HYPODERMIC MEDICATION

BARTHOLOW

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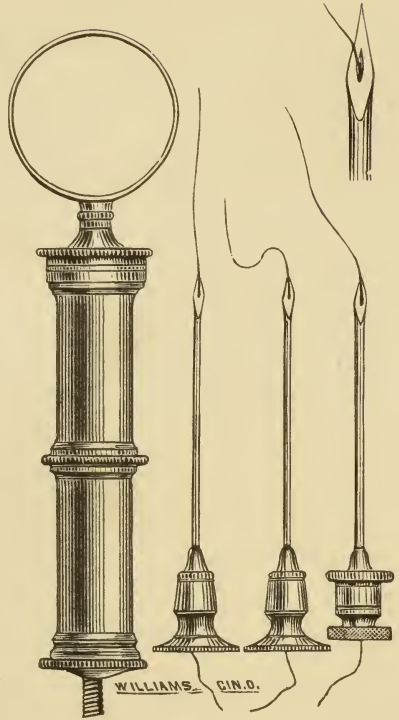
MANUAL

OF

HYPODERMIC MEDICATION.



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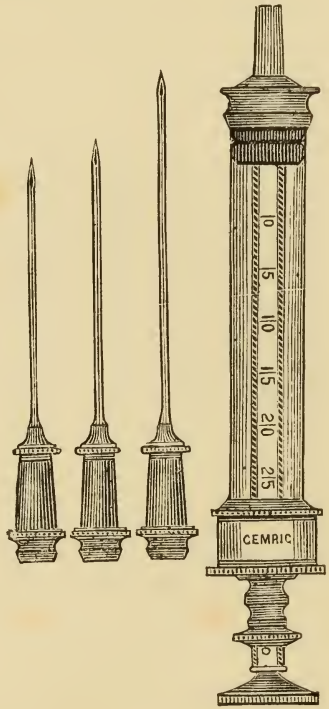

No. 3.

No. 1. Author's Silver Hypodermic Syringe. No. 2. Rimmers for cleaning Needles.

No. 3. Glass Hypodermic Syringe (Gemrig).

MANUAL

OF

HYPODERMIC MEDICATION.

BY

ROBERTS BARTHOLOW, A.M., M.D.,

Professor of Materia Medica and Therapeutics in the Medical College of Ohio; Lecturer on Clinical Medicine and Physician to the Hospital of the Good Samaritan; Lecturer on Morbid Anatomy and Pathologist to the Cincinnati Hospital; Author of the Russell and Jewett Prize Essays, of the National Medical Association Prize Essay on Atropia, for 1869, of the Fiske Fund Prize Essay on the Bromides, for 1869, etc. etc.

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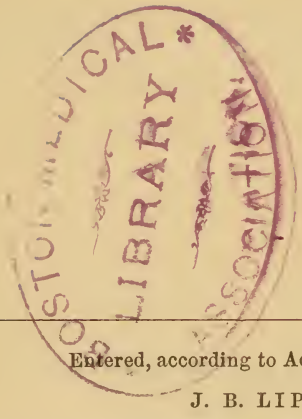

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DEDICATED

TO

ANDREW HULL BAKER, A.M.,

PRESIDENT OF CALVERT COLLEGE, MARYLAND,

BY HIS OBLIGED FRIEND

AND

FORMER PUPIL,

THE AUTHOR.

Je pense même, à raison de ces circonstances, que l'absorption sous-cutanée, qui n'a été employée jusqu'ici sur l'homme que par exception, devra devenir méthode générale pour l'administration de tous les médicaments énergiques, et à l'état de pureté.

Bernard.

Who that has suffered from a painful local affection can think of the alleviation of his sufferings which follows from the subcutaneous injections of an anodyne without gratitude?

Sir W. Jenner.

PREFACE.

As a teacher of Therapeutics, and as a practitioner, it has frequently been brought to my notice that the information existing in our language on the subject of hypodermic medication is exceedingly meager. I have been urged by students and practitioners to prepare a convenient manual, to embody in small compass what is really known of value on this subject. This little work is the result.

Those who do me the honor to read my book will find that I have drawn largely upon my personal experience in the use of the hypodermic method. This fact, together with the necessity I was under not to enlarge my work beyond the boundaries of a "manual," will, I trust, excuse the apparent dogmatism of my statements. As, however, the experience and observation of one individual, how great soever may have been his opportunities, must necessarily, in so extensive and important a subject, be incomplete, I have not neglected the contributions of English,

French, and German physicians to this department of practical medicine.

I am indebted to the present resident physicians of the Good Samaritan Hospital for important aid. Drs. De Courcey and Rutter, with a scientific zeal which does them honor, submitted themselves to experiments in order to elucidate some important points in the physiological action of morphia and atropia. Dr. Galbraith made and recorded the observations.

Dr. J. S. Unzicker, of this city, a very capable physician and pharmaceutist, has placed me under obligations for numerous careful experiments, to determine what agent, if any, is best suited to prevent change in solutions prepared for hypodermic use.

R. B.

CINCINNATI, OHIO.

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MANUAL

OF

HYPODERMIC MEDICATION.

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PART I.

History, Technology, and General Therapeutics.

I.

HISTORY.

THERE are two important epochs in the history of hypodermic medication:

1. The discovery of the practicability and utility of introducing medicines under the skin for the relief of local pain.

2. The subsequent demonstration that the physiological and therapeutical effects of medicines thus administered are procured through the agency of the blood, and that "localization" of the injection is not necessary.

We are indebted for the first discovery to Dr. Alexander Wood, of Edinburgh, and for the second to Mr. Charles Hunter, of London.

Dr. Wood ascertained, in 1843, that a solution of morphia injected under the skin, in the vicinity of a painful part, afforded remarkable relief to the pain.

His first publication on the subject was made in 1855, in the *Edinburgh Medical and Surgical Journal.* The prior claims of Dr. Wood have been disputed by Mr. Rynd, of Dublin, for himself, and by Dr. Sieveking, of London, for Kurzak, of Vienna.* Mr. Rynd affirms that "the subcutaneous injection of medicinal substances, to combat neuralgia, was first used by himself in Meath Hospital, in 1844." It appears, however, that Dr. Wood's method was known and practiced in Edinburgh as early as 1843. Dr. Sieveking asserts that "Dr. Kurzak, of Vienna, was the first to employ the subcutaneous or hypodermic method, which was then largely used by Dr. Wood, of Edinburgh." If this statement be correct, it is not a little remarkable that the German writers on this subject do not advance the claims of Dr. Kurzak to priority of discovery. I am unable to find in the works of Erlenmeyer,† Lorent,‡ and Eulenberg,§ any mention of Kurzak's claims; on the contrary, these authorities award to Dr. Wood the honorable distinction of being the author of the hypodermic method.

Although the remote or systemic effects produced by subcutaneous injections were observed by Dr. Wood, he nevertheless attributed the curative power to the

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* *Lancet*, 1861, vol. i. p. 309.

† Die subcutanen Injectionen der Arzneimittel, von Dr. A. Erlenmeyer. Neuwied und Leipzig, 1866. Dritte Auflage, p. 1.

‡ Die hypodermatischen Injectionen nach clinischen Erfahrungen, von Dr. E. Lorent, in Bremen. Leipzig, 1865, p. 1.

§ Die hypodermatische Injection der Arzneimittel, etc. von Dr. Albert Eulenberg. Berlin, 1867, p. 10.

local action of the substance injected. "The local effect depends," he informs us, "much upon the affinity between the particular medicine administered and the tissue to which it is applied." In accordance with this view of the *modus operandi*, he directs that "the instrument is not to be put into the place where the patient complains of pain, but into the spot where you find you can awaken the pain on pressure,"—the painful points of Valleix. That Dr. Wood was not unobservant of the remote or systemic effect of subcutaneous injections is evident in the following remarks:

"It is truly astonishing how rapidly it affects the system. If you throw in a large quantity (of morphia), you will see the eyes immediately injected and the patient narcotized, and in a few minutes afterward you will see him in a profound sleep."

It was reserved for Mr. Charles Hunter to demonstrate the important fact that the application of the injection to the painful points, as contended for by Wood, was really unnecessary, and that equally good effects followed the introduction of the injection into a distant part. Mr. Hunter's first paper appeared in 1859, and was entitled "Experiments relative to the Hypodermic Treatment of Disease." These experiments, made on animals, demonstrated that hypodermic injections "acted by absorption; that they acted quicker than by the endermic method, or than stomachic doses; that they acted more effectually; and that a small injected dose was equivalent to a much larger one by the stomach." Mr. Hunter was permitted to use the method of Wood on two patients afflicted with neuralgia, in care of Dr. Pittman in St. George's Hos-

pital. As "both had abscess in the neuralgic site, from the continuance of the localization," the point of introduction of the injection was varied, and it was found — "First, that in neuralgia equal benefit followed distant injection of the cellular tissue as followed the injection of the neuralgic site; secondly, that localization was not necessary to benefit a given part; and thirdly, that for certain reasons it was better not to localize—the chief being: 1, The infliction of unnecessary pain; 2, the almost certain risk of irritating, thickening, or inducing matter in the part from repetition; and 3, it became evident that a large class of neuralgia would be excluded from this treatment if it was necessary to inject the neuralgic site."

Great praise must be awarded Mr. Hunter for his success in demonstrating these important conclusions, and for popularizing his method. His industry in collecting facts and presenting them to the profession was indefatigable. His views were perseveringly advanced, —not always in very correct or elegant English, as the reader will observe,—but with an intelligent appreciation of the nature and importance of his facts. He read papers before societies; he published articles in the *Medical Mirror*, *Lancet*, *Medical Times and Gazette*, and *British and Foreign Medico-Chirurgical Review;* he issued a pamphlet* containing all of his previous papers and some additional facts, and he enlisted, by personal effort, many of the physicians and sur-

* On the Speedy Relief of Pain and other Nervous Affections by means of the Hypodermic Method. Churchill, London, 1865.

geons of London in a trial of the new therapeutical expedient.

It was thus, chiefly through the efforts of Mr. Hunter, that the method of Wood, previously confined to Edinburgh and to Dublin, became naturalized in England. Mr. Hunter's papers in the *Medical Times and Gazette* attracted the attention of Courty, of Montpellier, and Béhier, of Paris, who popularized the new method in France. It was soon after tried and reported upon favorably by Scanzoni, of Wurtzburg; Oppolzer, of Vienna; Graefe, of Berlin, and numerous other eminent authorities on the Continent. In 1865 a small treatise, by Dr. Lorent, of Bremen, appeared at Leipsic. A monograph, by Dr. Erlenmeyer, passed to the third edition in 1866. In 1867 the second edition of the elaborate work of Dr. Albert Eulenberg was published in Berlin. Dr. Eulenberg gives a list of two hundred and twenty articles and essays in various languages, but chiefly in German, which appeared on this subject from 1855 to the date of publication of the second edition of his work. From these facts may be seen the extraordinary extension which has been given to this method of treatment on the Continent.

The method of Wood, as illustrated by Hunter, met with a more favorable reception on the Continent than in the country of its origin. According to Dr. Anstie,* "it is still very much unappreciated" in England. It is true that the principal English physicians and surgeons think highly of the method, and now employ it largely, but, as Dr. Anstie informs us, there are "prac-

* The Practitioner, July, 1868.

titioners who will not admit that there *can* be any particular advantage in it which the old way of giving medicines does not offer."

Similar prejudices exist in this country. Those who employ the hypodermic method are largely in the minority. Some oppose it because it is an innovation upon an old method; others can see no advantage it has over the stomach administration; others still, unacquainted, in a practical way, with the mode of using it, are afraid of its power. The hypodermic method was, however, early practiced in this country. So long ago as 1860, Dr. Ruppaner, of Boston, called the attention of the medical profession in this country to the great value of the hypodermic method in the treatment of neuralgia.* Articles, more or less extended, have appeared in medical journals from Drs. Storer and Warren, of Boston, Reeve and McElroy, of Ohio, Dickson, Hutchinson, Mitchell, and others, of Philadelphia, Catlin, of Connecticut, and in the transactions of the Medical Societies of Pennsylvania, of New York, and of Ohio, and in the works of Stillé, Biddle, and Wood.

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* Besides his articles in the Boston Medical and Surgical Journal, Dr. Ruppaner issued, in 1865, a special treatise on "Hypodermic Injections." Burnham, Boston, 1865, pp. 160.

II.

TECHNOLOGY.

Mr. Hunter proposed the term *hypodermic* in 1859, to make the terminology uniform with that already in use. The word is compounded of two Greek words, ὑπο, *under*, and δερμα, *the true skin*. By this method, then, the medicine is introduced not *into*, but *under*, the true skin, into the subcutaneous areolar tissue. This does not include the method of inoculation as practiced by Lafargue, nor the injection of irritants into diseased tissues, as proposed by Luton* and further illustrated by Bertin.† The method of Luton has, however, sufficiently close relationship with the hypodermic method, and possesses of itself sufficient value, to justify me devoting a short chapter to it.

The subcutaneous method proper consists of two elements:

The medicine in a state of solution.

An instrument for injecting the solution into the subcutaneous areolar tissue.

The Solution.—A medicine employed for hypodermic use should be capable of perfect solution in the vehicle, which is usually distilled water. Particles of medicine undissolved are not only not in a condition to be readily absorbed, but act as irritants to the tissue, producing inflammation and abscess.

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* Archives Générales de Médecine, Oct. 1863.

† Ibid., Avril, 1868, p. 444.

The solution should be free from dirt or foreign matter of any description.

The solution should be neutral, or, at least, without decided acid or alkaline property.

Any substance which will coagulate the blood, or produce violent irritation, is unfit for hypodermic use.

A solution, even of a neutral substance, should not be too concentrated. Pure distilled water is entirely harmless, and the quantity of fluid injected is, within certain limits, a matter of indifference, provided suitable care be used in selecting the site and in injecting. Concentrated solutions, *cæteris paribus*, are more apt to produce local irritation than dilute solutions. Moreover, if the solution of a powerful alkaloid be very concentrated, a drop too much injected may produce dangerous symptoms. In ordinary syringes, a few drops remain at the bottom of the cylinder and in the needle; hence it is difficult, in using a very concentrated solution, to inject the precise amount desired, or, indeed, to approximate to it very closely.

Solutions of alkaloids too long kept become unfit for hypodermic use, by reason of the development in them of a *penicillum*. This organism grows at the expense of the alkaloid, and hence the solutions diminish in strength as the parasite develops. I have tested the utility of the various agents which may be employed to prevent the development of this penicillum, but have not arrived at a satisfactory result. Carbolic acid, alcohol, alum, and acetic acid, unless added to the solution in quantity sufficient to prove irritant, have not succeeded, after a sufficiently prolonged trial. The mineral acids are effective, but they confer such

irritant properties on the solution as to render its use very painful, as well as injurious. The proper method is to prepare fresh solutions as often as may be necessary, and in such quantities as the exigencies of practice may require.

I cannot too strongly urge upon the practitioner the expediency of preparing the solutions himself. The *material* required is not expensive, the processes are simple, and the confidence which comes of personal knowledge of the accuracy in the proportions is of advantage in handling the remedy. The apparatus required for this purpose consists of the following articles:

A fine grain druggist's balance.

A small glass or Wedgewood mortar.

A small glass funnel.

Fine Swedish filtering paper.

Pure distilled water.

The medicine, solution of which is to be made, is to be finely triturated in the mortar, and the distilled water gradually added, with continuous stirring. When the solution is made, or before being used, it should be passed through the filter. Before the filter is used for purifying the solution, distilled water should be passed through it, to carry off loose particles of paper and dirt which may have collected in the funnel. When prepared, the solution should be preserved in carefully stoppered vials. Stoppers of cork are unsuitable, owing to the friable nature of that material.

The practitioner should provide himself with ounce vials, having ground-glass stoppers, for containing the solutions ordinarily in use. They should be carefully labeled with name of alkaloid, the quantity to the ounce, and the proper dose.

The Instrument.—The instrument for introducing the solution under the skin consists of a syringe, the nozzle of which is a perforated needle. The syringes first employed were crude instruments. Not being provided with a needle point, a preliminary incision through the skin was necessary in order to introduce the canula. (Instrument of Wood, and the Pravaz syringe.) Mr. Rynd, of Dublin, invented a complicated apparatus for introducing the solution under the skin, the fluid flowing out by the force of gravity. Mr. Hunter's syringe is thus described by himself: "The barrel is of glass with silver fittings, and contains a piston which works by a screw-rod, each half turn of which expels half a minim as a fine drop at the end of the pipe. Two pipes belong to each syringe, the one larger and stronger than the other. . . . The smaller pipe will be found the best for general use; it screws on and off the barrel at pleasure, and is made of silver with a hardened gold point. The point is sharp like a needle, and perforated on one side by an oblique opening."

The syringe of Pravaz, as modified by Béhier, is much used in France. This is very similar in construction to Mr. Hunter's; it is of glass; the piston works with a screw, and the needle is attached by a screw to the barrel. The syringe of Mathieu, known as the "decimal hypodermic syringe," and graduated according to the French metrical system, is also a modification of that of Pravaz. The instrument of Lüer, which is most popular in Germany (Eulenberg), is graduated on the flat side of the semi-cylindrical piston-rod, and has a set screw, which can be used or not. The needle fits accurately by a socket-joint, without

being screwed on, and has a lancet-shaped point, slightly concave on its perforated side to facilitate transfixing the skin. The Committee on Hypodermic Medication of the Medico-Chirurgical Society* recommended Coxeter's, Whicker and Blaise's, and Weiss's syringes. I am familiar with the instrument of Weiss only. This has a glass cylinder, screw-piston, is graduated, and has a capacity of thirty minims. Dr. Anstie thinks "the ideal syringe, perhaps, is a Coxeter, with the addition of a screw-joint, by which the barrel can be removed and refilled without withdrawing the canula from the skin."

In this country a modification of the Pravaz instrument, imported from France, is found in the shops. It has a glass barrel, graduated, and having a capacity of thirty minims. The piston works, with or without a screw, by means of an auxiliary screw attached, not to the mountings, but to the piston itself. It contains two gold-plated needles, differing in size, and they fit to the barrel accurately by a socket-joint, and do not screw on. Although any of these instruments may perform, more or less satisfactorily, the work required of them, they do not equal, in the judgment of the author, the instrument to be presently described. There are two strong objections to an instrument of glass.

The mountings work loose and readily give way, unless connected by lateral supports, as in the Charrière syringe.

The glass cylinder breaks easily, especially if graduated.

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* Medico-Chirurgical Transactions, vol. l. p. 564.

The advantages of a glass instrument are these:

The cylinder may be graduated.

The contents are visible to the eye.

Cheap instruments of hard rubber are also in use. They quickly get out of order, and are much inferior in construction to the fine English, French, and German syringes mentioned above. Nevertheless, a hard rubber syringe may be preferred for the injection of certain minerals.

After considerable experience and no little vexation in the use of various kinds of instruments, I do not hesitate to declare my preference for the silver hypodermic syringe. It is made of pure silver, and has a capacity of thirty minims. It contains two silver needles of different sizes, and also a trocar, which screw on to the barrel. The needles are somewhat lancet-shaped, and readily perforate the skin. The piston does not work with a screw; it is packed with leather, and accurately fits the barrel. The lower extremity of the piston is filled in with a silver plate, which closely adapts itself to the bottom of the cylinder, in order to insure the expulsion of all the fluid. The piston-rod may be graduated, but I prefer to use a minim-glass. The piston of this instrument works so accurately that every drop in the minim-glass may be drawn up into the barrel by aspiration, and all may be injected except the small portion which remains in the needle.

The advantages of the silver hypodermic syringe are these:

It is not readily broken.

It will wear indefinitely.

It performs the required work in a satisfactory manner.

Nothing is more certain, however, than that carelessness will render useless the best instrument. Some details, therefore, with regard to the care of a hypodermic syringe will not be considered superfluous.

The leather packing must be kept well oiled, and so spread out that when the piston is forced down, the orifice of exit being closed, air cannot pass the piston. If the leather be permitted to become dry and shrink, the instrument will be unfit for use, and possibly at a time when its use might be urgently demanded. The cylinder should be frequently washed out with pure water, to insure that it is free from undissolved medicine and particles of dirt. The needles must be wiped dry after use, and the fine wire with which they are accompanied must be introduced. If long disused, the needles rust and become closed. There should accompany each hypodermic syringe a *rimmer*, an instrument for cleaning out the needles when obstructed. The possibility of communicating disease by inoculation of specific matter should not be overlooked.

There are several methods by which the hypodermic syringe may be charged with the required dose of the solution. The fluid may be drawn up into the barrel by aspiration, the cap of the barrel may be unscrewed, the piston removed, and the solution poured into the barrel. The former is more convenient. If air enter when the fluid is being drawn up, it may be readily expelled by inverting the barrel and moving up the piston until a drop of the fluid presents itself at the orifice of the needle. In using a glass instrument which is graduated, more of the solution should be drawn into the barrel than it is contemplated to administer, and,

fixing the eye upon those divisions of the scale representing the amount to be injected, the piston is made to traverse slowly the proper space. In filling my silver instrument I pursue the following method: I pour into a minim-glass the proper quantity of the solution. The needle being screwed into its place, I insert the point into the solution and draw the whole amount into the barrel of the syringe by slowly elevating the piston, inclining to one side the minim-glass, in order to take up the last drop. If air have entered, I invert the syringe and push up the piston slowly until it is all expelled. An allowance of one minim should be made for loss.

The mode of injecting, which is very simple, is as follows:

Take up between the thumb and forefinger of the left hand a loose fold of skin in some convenient situation. Push in the needle, with a quick and decided motion, at a right angle to the direction of the fold. The resistance ceasing, it will be known that the needle has perforated the skin, and the point of the needle may also now be freely moved about in the subcutaneous areolar tissue. It is better to pass the needle for an inch or more under the skin, to have sufficient space for the fluid. The injection must be made slowly, drop by drop, so that the fluid may diffuse itself without rupturing any small vessels, or the fibers of the connective tissue. When all has been injected, withdraw the needle slowly, pressing at the same time upon the puncture to prevent escape of the fluid. A few minutes' pressure will suffice to retain the fluid, and to arrest the little bleeding which sometimes takes place.

A bit of isinglass plaster may also be applied to the puncture, but this is generally unnecessary. By some persons the fluid is always injected into a muscle; and this is the method of using strychnia in paralysis, but is not frequently adopted for other agents employed hypodermically. To inject into a muscle, for example, the brachialis anticus, make it tense by flexing the forearm, and then by a quick motion thrust the needle directly into the muscle. It is claimed for this method that it is less painful and less liable to be followed by abscess than by the injection under the skin, but it is obviously improper if any considerable amount of fluid is to be injected.

In practicing the hypodermic injection, it is important to avoid puncturing a vein. Serious depression of the powers of life, fainting, and sudden and profound narcotism have been produced by injecting a solution of morphia directly into a vein. Fatal collapse might be induced by injecting air into a large vein along with the solution.

Bony prominences should also be avoided, for in these situations the skin is not sufficiently loose to permit the ready entrance of the fluid, and inflammation and abscess will follow a too forcible injection.

The puncture should not be made, as a rule, into inflamed parts. I have known a bad phlegmon produced by injection into the tissues of an inflamed wrist.

It is not necessary to follow the original method of Wood, and inject into those points in which pain can be awakened by pressure. Some exceptions to this rule undoubtedly exist, as will hereafter be shown, but they are not numerous. The arm, the outer face of the

thighs, the calves, the abdomen, and the back are suitable places for the injection. The arm, about the insertion of the deltoid, is generally selected. Eulenberg makes the assertion that the effect is slower when the injection is made in the back than in any other situation.* I have not been able to observe any difference in the rapidity of effect as influenced by the site of the puncture. If, as sometimes happens, the patient prefer injection into the painful part, it will be well to yield to his prejudices, provided no contraindication exist thereto.

If the patient be timid, and intolerant of pain, the sensibility of the skin may be lowered by ether or rhigolene spray. A piece of cotton cloth moistened with chloroform and held on the skin a few minutes is nearly as effective as the douche, and much more convenient. Sometimes redness and swelling take place at the site of the injection. This is best relieved by a cold wet compress.

The syringe, half-ounce glass-stoppered vials, containing the solutions most frequently used, and minim-glass, should be contained in a small leather pocket-case, at all times ready for use.

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* Die hypodermatische Injection, etc , op cit. p. 62.

III.

GENERAL THERAPEUTICS.

A REMEDY administered by the stomach is affected in its physiological and therapeutical action by the condition of that organ. Disease, as for example gastric catarrh, limits, if it may not entirely prevent, the absorptive action of the mucous membrane. Also, the state of repletion of the veins, the presence of other ingesta, and the condition of annexed organs influence the rate and extent of absorption. The digestive fluid undoubtedly exerts a chemical action upon many remedial agents, thereby retarding, limiting, or preventing their physiological and therapeutical activity. Lastly, many agents, of the narcotic class especially, depress the nerves of the stomach, and, in this way, affect the rate and degree of absorption. On the other hand, when a medicine suitable for the purpose is thrown under the skin, its physiological and therapeutical effects are produced in the fullest degree and in the most characteristic form. It follows, then, that the therapeutical powers of a drug must not only differ in degree, but also in kind, according as it is given by the stomach or injected under the skin. Experience and observation demonstrate the truth of this statement. The subcutaneous use of certain drugs has developed very valuable therapeutical properties, which the stomachic administration had not even suggested. Ber-

nard* affirms that this mode of administering remedies, which has hitherto been the exception, must become the general method for the use of the active principles. The advantages of this method over other methods, considered from the point of view of practical therapeutics, are manifold.

The effect is produced more speedily, and the whole effect of the quantity introduced.

The results are more permanent and curative.

Gastric disturbance rarely occurs, and irritation of the stomach is avoided.

The administration may be made to persons unwilling or unable to swallow.

It follows, then, that remedies suitable for this purpose may be used hypodermically, to produce

1st. All of the physiological and therapeutical effects which can be accomplished by them when given by the stomach; and

2d. The physiological and therapeutical effects peculiar to this method.

The hypodermic method may be employed for

1st. A local action only.

2d. The general or systemic effects.

LOCAL EFFECTS.

To cure nævi, aneurisms, varicose veins, etc. by coagulating the blood (liq. ferri subsulphatis; liq. ferri perchloridi, etc.).

To destroy morbid growths, goitre; or irritant injections into substance of tumors (tinct. iodinii iod.). (Acetic acid in cancer, etc.)

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* Archives Générales, 1864.

REMOTE OR SYSTEMIC EFFECTS.

As a cerebral sedative.....	In Insomnia. Melancholia. Mania. Puerperal mania. Delirium tremens, etc.
As a moderator of reflex action.....	In Epilepsy. Chorea. Eclampsia. Hysteria. Tetanus. Hydrophobia, etc.
As a motor excitant.....	In Paralysis, etc.
As an anodyne.....	In the various forms of neuralgia, etc.
In affections of thoracic viscera.....	Spasmodic cough. Hooping-cough. Asthma. Angina pectoris. Bronchitis. Pleuritis. Pericarditis, etc.
In affections of digestive system.....	Dyspepsia. Vomiting of pregnancy. Sea-sickness. Cholera morbus. Colic. Intussusception. Enteritis. Peritonitis. Hepatic colic. Schirrus, etc.

In affections of the genito-urinary apparatus.....	Dysmenorrhœa. Uterine colic. Nephritic colic. Spasmodic stricture. Spasm of sphincter vesicæ. Spermatorrhœa. Chordee, etc.
In fevers....	Periodical fevers, etc.
In blood diseases.....	Rheumatism. Syphilis, etc.
As an antidote.....	Opium. Belladonna. Strychnia. Physostigma, etc.

To produce the effects embraced in the above tabular statement, a number of remedial agents have been employed by the hypodermic method. As I have already indicated in my remarks on solutions, drugs in a crude state are not in a sufficiently active and soluble form for this mode of administration; hence the active principles are chiefly used.

The following agents have been employed hypodermically:

Source.	*Preparation for Subcutaneous Use.*
Opium. (Papaver Somnif.)	Tincture; Acetated Tincture. Extract; Liq. Opii Comp. (Ruppaner.) Morphia and its salts. Narceia. Codeia. Narcotina. Thebaina.

Belladonna. (Atropa Belladonna.)	Atropia and its salts.
Hyoscyamus. (Hyoscyamus Niger.)	Hyoscyamia. Tincture.
Stramonium. (Datura Stramonium.)	Daturia.
Coffee. (Caffea Arabica.)	Caffein.
Tobacco. (Nicotiana Tabacum.)	Nicotia.
Aconite. (Aconitum Napellus.)	Aconitia.
Conium. (Conium Maculatum.)	Conia.
Colchicum. (Colchicum Autumnale.)	Colchicia.
Nux Vomica. (Strychnos Nux Vomica.) Woorara.	Strychnia and its salts.
Digitalis. (Digitalis Purpurea.)	Digitalina.
Veratrum. (Veratrum Album.)	Veratria.
Ergot. (Secale Cornutum.)	Ergotina. Ergotin.
Calabar Bean. (Physostigma Venenosum.)	Extract; Physostigmia.
Hydrocyanic Acid.	
Cinchonia.	Quinia and its salts.
Ipecacuanha. (Cephaëlis Ipecac.)	Emetia.
Iodine.	Tincture; Iodide of Potassium.
Sodium.	Chloride.
Ammonium.	Chloride.
Iron.	Liq. Ferri Subsulphatis.
Copper.	Sulphate.

Silver.	Nitrate.
Mercury.	Corrosive Sublimate. Biniodide.
Arsenic.	Liq. Sodæ Arseniatis.

Many of these agents have either proved unsuitable for subcutaneous injection or are inefficient. In the following pages I propose to consider those the utility of which has been established by experiment and clinical observation. They are the following:

Morphia and its salts.
Atropia and its salts.
Strychnia and its salts.
Conia.
Woorara.
Physostigma.
Caffea.
Nicotia.
Hydrocyanic acid.
Quinia and its salts.
Ergot.
Iodide of potassium; tincture of iodine.
Subsulphate and perchloride of iron.
Arseniate of soda; Fowler's solution.

In practice it will be found that this list may be much reduced. For the ordinary contingencies of medical practice, the following only are necessary:

Morphia (sulphate).
Atropia (sulphate).
Strychnia (sulphate).
Quinia (sulphate).

The physician's hypodermic case should contain solutions of morphia, atropia, and strychnia.

PART II.

Special Therapeutics.

I.

MORPHIA.

THE SOLUTION.—There is no general agreement as to the salt of morphia best adapted to hypodermic use. As the sulphate is the most soluble salt, this should be preferred. In Germany, the hydrochlorate is much used. The formula of Eulenberg* is as follows :

℞.—Morphiæ hydrochlorat. gr. iv ;
Acidi hydrochlor. gutt. iv ;
Aquæ destill. ʒi. M.

In this formula the muriatic acid serves a double purpose : it increases the solubility of the morphia, and it prevents the development of the *penicillum.* But acid solutions, as I have already pointed out, increase the pain and smarting which attend the injection, and not unfrequently produce inflammation and abscess. The Committee of the Medico-Chirurgical Society, in their experiments, used the acetate of morphia dissolved by the aid of sufficient acetic acid, and afterward neu-

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* Op. cit.

tralized with liquor potassæ. The Committee wisely remark: "In using drugs which require an acid to render them soluble in water, it was found that very acid solutions were apt to irritate, and the solutions were therefore carefully neutralized." Would it not have been better to use a salt of morphia readily soluble in water without the aid of an acid, the more especially as the Committee had ascertained that pure water occasioned very little irritation?

Dr. Anstie, in a very valuable paper on "The Hypodermic Injection of Remedies,"* says that "morphia should be used in the form of acetate dissolved with a minimum of acetic acid in hot distilled water, five grains to the drachm." This solution, it appears to the writer, is objectionable in several respects. It is too concentrated; one minim containing one-twelfth of a grain,—a quantity difficult to inject with accuracy by an ordinary syringe. Dr. Anstie himself states another objection: "As the salt varies in solubility, it will often happen that on cooling the solution will solidify: this is not of much consequence, as it can be heated in hot water at the moment of use." (?)

I prefer a simple solution of the sulphate, according to the following formula:

℞.—Morphiæ sulphat. gr. xvi;
Aquæ destill. ℥i. M.
Dissolve and filter.

The morphia should be rubbed up in a mortar and the distilled water added gradually. A perfect solution

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* The Practitioner, July, 1868.

will be obtained, which does not require an acid. Fifteen minims represent half a grain; five minims a sixth of a grain.

Dose.—The dose of morphia for hypodermic use varies from $\frac{1}{12}$ to $\frac{1}{2}$ of a grain. *In commencing it should not exceed one-third of that ordinarily administered internally.* It is prudent in all cases to test the physiological capabilities of the patient by a moderate dose, before resorting to the maximum amount. Patients vary in their susceptibility; women are, as a rule, more easily affected than men. Five minims of my solution — one-sixth of a grain — is a sufficient dose for many of the conditions requiring an injection. Persons habituated to the use of the drug, and those suffering pain, will bear a larger quantity. The maximum doses may be administered with safety if combined with atropia (see post). As Brown-Séquard has indicated, large doses of morphia when combined with atropia exert a more decided curative effect in obstinate neuralgias. It may be necessary in such cases to give $\frac{1}{2}$, and even 1 grain of morphia, with $\frac{1}{48}$ of a grain of atropia.

In order to maintain a constant physiological effect but slight increase of the dose is necessary. This is one of the greatest advantages of the hypodermic method, especially in cases requiring the protracted use of morphia.

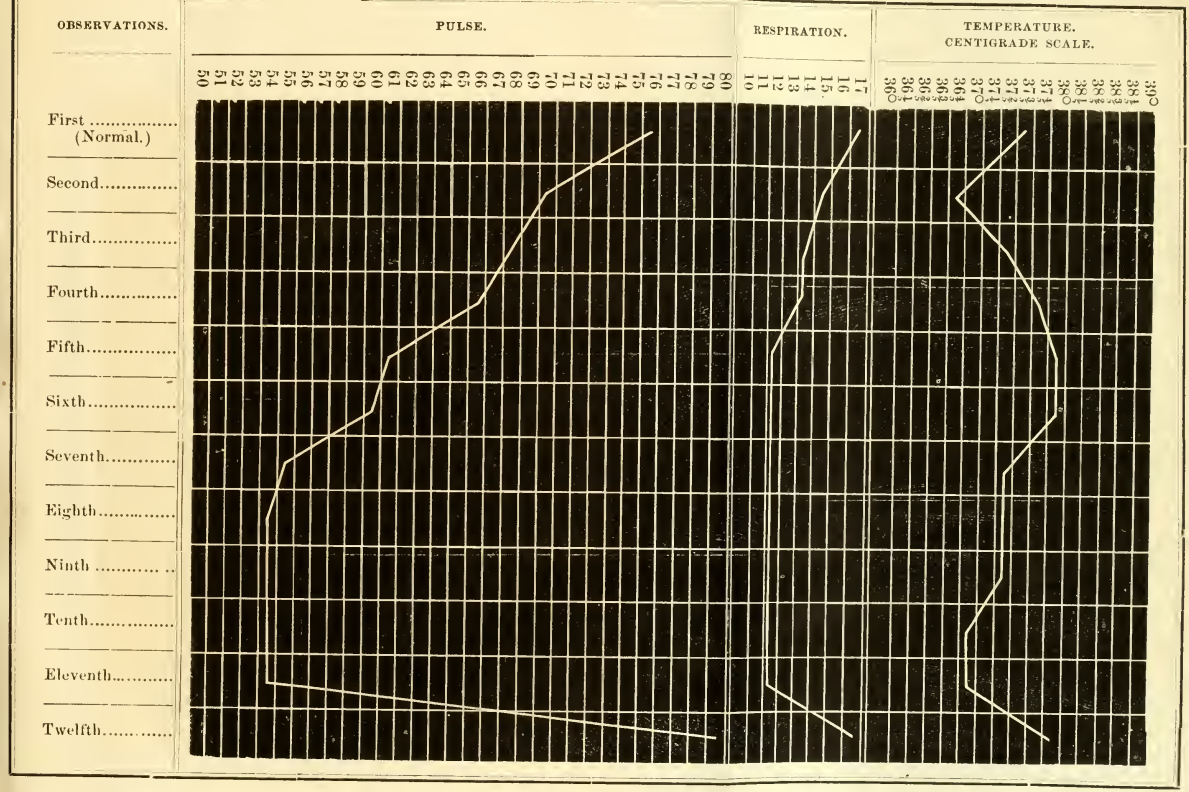
Hypodermic injections of morphia are rarely advisable in the case of children, yet, as their utility is unquestionable in certain convulsive disorders of early life, it may be necessary to employ them. From $\frac{1}{30}$

to $\frac{1}{10}$ of a grain, according to age, is a sufficient dose. I have not ventured to use the injection in children under three years of age.

As the quantity proper to be administered is differently stated by different authorities, I desire to impress upon my readers the necessity for caution. The large doses sometimes recommended—$\frac{1}{2}$, $\frac{3}{4}$, and even 1 grain—are unsafe for the first trial, unless the conditions requiring the injection be exceptional.

Physiological Effects.—When the solution is injected, a pain, compounded of smarting and burning, is experienced in the part, and this is followed by some itching. The tactile sensibility, and also the sensibility to pain, is diminished at the site of the injection. In a short period of time, varying from a few seconds to ten minutes, the systemic effects are felt by the patient. A sense of heat and of fullness in the face and head, giddiness, singing in the ears, and, in many persons, nausea, are experienced. Some abdominal pain is sometimes felt; and loud borborygmi not unfrequently occur at the moment the cerebral symptoms are perceived. The vertigo impairs the voluntary control, and walking becomes uncertain, difficult, or impossible. With the manifestation of these cerebral effects, injection of the conjunctivæ and more or less contraction of the pupils occur. The face is also flushed. The mouth becomes pasty, the tongue dry, and the taste perverted by reason of the dryness of the epithelium. Deglutition is, also, somewhat painful and difficult, owing to the same condition of the mucous membrane. The special sense of hearing becomes much more acute than normal. With the development of these physiological

*Observations made every half-hour on Dr. H. C. Utter after taking hypodermically one quarter of a grain of sulphate of morphia.



effects, pain, cramp, and spasm are relieved, or are borne without suffering, for a feeling of comfort and content, difficult to describe, takes possession of the mind. A condition of somnolence in many persons, in others of extreme wakefulness characterized by intense activity of the mind, is experienced. If sleep occur it is usually deep, the respiration being slow and labored. In some instances the sleep is disturbed by dreams and visions,—a somnambulistic state from which it is difficult to arouse the patient.

Characteristic influences are exerted upon the great functions of colorification, circulation, and respiration. It was Mr. Hunter* who first pointed out the effect of the subcutaneous injection of morphia in lowering the pulse. He informs us that "in mania he had reduced the pulse from 120 to 80 in four minutes." He observed, also, "the diminished rate of respiration."

In order to exhibit these effects I have constructed the annexed diagram of the pulse, temperature, and respiration movements.

Soon after the injection, more or less decided itching of the nose, and in many persons during the time the morphia narcosis is at its maximum, an irritation of the whole cutaneous surface, are experienced. This effect is usually followed by general diaphoresis,—the sweating being in many instances very profuse.

With the development of the morphia narcosis there occur dryness of the mouth and fauces and an arrest of secretion in general, except that of the sudoriparous glands. If the injection be administered after a full

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* On the Speedy Relief of Pain, etc., op. cit. p. 33.

meal, digestion is suspended, the food remaining unchanged in the stomach for several hours. As a rule, constipation results; but to this there are numerous exceptions, for in some instances I have known the peristaltic movements to be actually increased. In common with the other organs, and possibly, also, in consequence of the diaphoresis, the functional activity of the kidneys is lowered, and the amount of urine secreted is much below the normal. More or less difficulty is experienced in the emission of urine; when the desire is felt, a long interval elapses before the flow takes place, and, as the contractile power of the bladder and of the ejaculatory muscles is diminished, the emission of urine is slow.

With the decline in the morphia narcosis, some patients experience headache, confusion of mind, anorexia, and nausea, but these results are not so constant as after the internal use of this agent. If the injection be administered at night, the nausea and vomiting are experienced on rising in the morning. Perfect quiet, a cup of hot coffee taken before rising, an ice bag to the cervical spine, a full dose of the bromide of potassium, may be administered for the relief of these symptoms when they are severe.

The extent and persistence of the foregoing physiological effects will depend upon the quantity of morphia injected. Very large doses excite not only immediate disturbance in the functions of the brain, but secondary disturbances in the process of elimination of the narcotic from the blood. The occurrence of these unpleasant and depressing effects of the morphia narcosis is an additional reason for cautious tentative ex-

periments in any case in which the physiological tolerance of this agent is unknown.

Phenomena somewhat different in character, as well as in degree, from those which I have described under this head, follow the subcutaneous injection of large doses. The following symptoms were observed by me after the injection of one grain of sulphate of morphia:

In ten minutes the patient had fallen asleep so soundly, sitting upright in bed, that he could not be aroused. At the end of an hour I found him in a state of profound narcotism, his pulse 50 and feeble; respiration 10 and labored, with stertor; skin cold and sweating; face pale and ghastly. The conjunctivæ were deeply injected; pupils minutely contracted, and insensible to the strongest gas-light. No reflex movements could be excited by touching the eyes, or by irritation of the fauces. These formidable symptoms were relieved by the subcutaneous injection of atropia, but the patient slept twenty hours. Great difficulty of micturition was experienced for twenty-four hours longer. Injection of the conjunctivæ, huskiness of voice, and some difficulty in swallowing persisted for forty-eight hours.

The effects of an ordinary dose, $\frac{1}{4}$ of a grain, continue from twelve to eighteen hours, according to the susceptibility of the patient. It follows, then, to maintain the morphia influence in any given case, two doses per diem will, generally, be sufficient.

Are there any ill effects produced by the long-continued use of morphia when injected under the skin? This is a practical question of considerable importance. I have not observed effects different in character from

those produced by the long-continued internal administration, except in one case. In this instance extreme volubility, complete insomnia and restlessness were induced by the subcutaneous injection of half a grain of morphia every four hours. This patient, the unhappy subject of uterine cancer, was advised by her physician to use for the relief of her pain the hypodermic injection of morphia. As the attendants of this woman used the syringe, they were prevailed on by the evident extreme suffering which she endured, to increase the dose to the point named. At the end of three months she began to be restless, and complained that the effect of the morphia was no longer the same. She could not sleep; her restlessness became extreme; her extremities and the muscles of her head and face were agitated by choreic spasms; her eyes were brilliant and constantly in motion; she talked incessantly, partly in a perfectly rational manner, and partly in a delirium of a busy but harmless character. Her hallucinations were agreeable, and her countenance exhibited no appearance of distress. Her pulse was 96; respirations 20. The quantity of morphia which this poor woman received was evidently too great; the brain was permitted no respite from the narcotic influence. If atropia had been combined with it, or if the doses had been less frequently administered, these effects had probably not supervened. After the regular daily use, in one case, of the hypodermic injection for four months, I had no difficulty in withdrawing it, by gradually diminishing the dose; and Eulenberg reports a case in which 1200 injections were used without injury to the patient.

THERAPY.—The subcutaneous injection of morphia may be used to relieve pain, to relax spasm, to subdue inflammation, to cure specific diseases, and to antagonize toxic agents. An anatomical arrangement seems best adapted to embrace all of the therapeutical facts under these several heads. Accordingly, I shall consider the uses of morphia in

Diseases of the Brain and Nervous System.
" " Respiratory and Circulatory System.
" " Digestive Apparatus.
" " Genito-urinary Organs.
" of Constitutional or Specific Origin.
In certain Surgical Diseases and Operations.
As a Physiological Antidote.

Diseases of the Brain and Nervous System.

Psychical Disorders.—Mr. Hunter was the first to indicate the utility and to employ the hypodermic injection of morphia in the treatment of *psychical disorders.* He enunciated an important truth in the following observations: "For derangements of the cerebral nervous system we have in the hypodermic method a means of treatment far superseding in its immediate efficacy any other mode of medication." In another place he further remarks: "In this class of cases (mania) a single dose, administered beneath the skin, will at once break the neck of the disease. It will often, at once, stop the delirium, correct the mental aberration, and remove the exhaustion."* Notwithstanding the striking advantages thus shown to result from the hypodermic treatment of mania, some years elapsed before

* On the Speedy Relief of Pain, etc., pp. 18 and 19.

it came to be employed. Indeed, so late as May of the present year, we find a distinguished asylum superintendent* repeating the expression of Dr. Anstie, "that despite the satisfactory working of the hypodermic method, and of the greatly increased power of handling remedies which it gives us, it is still very much unappreciated." Dr. Robertson believes that "this remark applies to the employment of the hypodermic injection of morphia in the treatment of mental disease." According to the same authority, Dr. Mackintosh published a paper in 1861 on "The Subcutaneous Injection of Morphia in Insanity," and the reports of the Somerset Asylum contain allusions to the advantages of this method. Lorent,† Erlenmeyer,‡ and Eulenberg§ support the observations of Hunter by their individual experiences. Maudsley,‖ who places opium at the head of all the remedies employed in the treatment of insanity, considers the subcutaneous injection of morphia "a valuable expedient." My own experience, which has been limited, however, is very favorable to the subcutaneous injection of morphia. In a case of acute melancholia, characterized by insomnia and intense restlessness, I found this method of treatment exceedingly useful. A grain of morphia reduced the pulse from 140 to 96, quieted the agitation, and procured sound and refreshing sleep.

Robertson in the paper referred to gives three typical

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* C. Lockhart Robertson, in Practitioner, May, 1869, p. 272.

† Die hypodermatischen Injectionen, etc., op. cit. p. 16.

‡ Die subcutanen Injectionen, etc., op cit. p. 28.

§ Die hypodermatische Injection, etc., op. cit. p. 154.

‖ Reynolds's System of Medicine, vol. ii. p. 60.

cases of different forms of insanity—recent mania, chronic mania, and melancholia—in which the hypodermic injection was successful. The indications for the employment of this method are the following :

Prolonged wakefulness.

Maniacal excitement.

Obstinate and persistent refusal of food, or drink, or medicine.

Destructive and suicidal tendencies.

Maudsley adds a caution here, which I transcribe for the benefit of my readers: "It will be well to have in mind that neither opium by the mouth, nor morphia hypodermically injected, will always quench the fury of acute mania, and that successive injections of morphia, followed by brief snatches of fitful sleep, have been followed, also, by fatal collapse." The evidences of the beneficial effect of the injection are the following :

Prolonged and healthy sleep.

Less excitement on awakening.

Illusions or delusions less strong.

Willingness to take food.

Absence of any tendency to collapse, although pulse, temperature, and respiration are reduced.

To produce the best results, larger doses than those I have indicated as proper in general are necessary in the treatment of mania. Hunter administered $\frac{1}{2}$ and 1 grain ; Robertson speaks of $\frac{1}{2}$ grain of the acetate of morphia injected every four hours, and in one case of 1 grain injected night and morning. In cases which have occurred under my observation, extraordinary tolerance of the morphia was exhibited ; and in that case to which

I have made special reference, 1 grain was found necessary to procure sufficiently prolonged sleep.

It is in the beginning of mania that the hypodermic injection of morphia is most conspicuous for good. The timely use of the syringe may avert this disorder in that critical period when the occurrence of unusual excitability and sleeplessness indicates that an outbreak is imminent. This observation is especially true of puerperal mania.

Delirium Tremens.—We owe to Mr. Hunter the first suggestion of the hypodermic treatment of *delirium tremens*. It was afterward employed by Ogle, Semeleder, Lorent,* Eulenberg,† Ruppaner,‡ and others. Dr. Anstie, in an able paper on "Alcoholism,"§ thus formulates his views as to the utility of this method:

"Opium should never be administered by the stomach, but always in the form of morphia hypodermically injected, in the dose of $\frac{1}{10}$ to $\frac{1}{4}$, or $\frac{1}{2}$ grain."

The treatment of delirium tremens has undergone a radical change within the past few years. This is well expressed in the following observations by Dr. Anstie:

"In former times—indeed, a very few years since—the notion universally prevailed that the delirious symptoms were owing to the exhaustion which was chiefly kept up by want of sleep; and, consequently, that the production of continuous sleep for several

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* Op. cit. † Op. cit.

‡ Hypodermic Injections, 2d ed., p. 132.

§ Reynolds's System of Medicine, vol. ii. p. 90.

hours was the sole and all-important means of cure. It was therefore the custom to ply the patients with larger and larger successive doses of opium, with the view of drowning the delirium in narcotic stupor. Great mischief arose from this wide-spread belief and practice. In the first place, it has often happened that the patient, without ever sleeping at all, has passed first into a condition of coma-vigil, next of stertorous breathing, and at last sunk, fairly poisoned with opium."*

I have quoted these strong but just expressions to warn my readers against the abuse of the hypodermic injection of morphia in the treatment of delirium tremens.

The following are the indications for the use of this method in this disease :

The condition of "horrors," or wakefulness, preceding delirium.

Excessive and uncontrollable vomiting of food, drink, and medicine.

Mild cases, in which there is little tendency to depression of the vital forces, and in which the assimilation of food proceeds satisfactorily.

It is contraindicated in severe and protracted cases, with great depression of the vital forces and non-assimilation of food.

Cases in which serious organic lesions of liver or kidneys have occurred.

Cases in which the delirium tremens is consecutive to traumatic or other serious lesion of brain.

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* Ibid., p. 88–9.

In **cerebro-spinal meningitis** opium is the best remedy, especially in the onset of that disorder, and, according to Radcliffe,* the hypodermic injection of morphia is the best method of administration. Erlenmeyer,† who appears not to have had any personal experience with the hypodermic use of morphia in this disease, refers to the experience of Bois. According to Eulenberg,‡ Niemeyer used this method as a palliative in an epidemic at Rastadt and Carlsruhe. It relieved the pain and cramps, and quieted the extreme restlessness (*grosse Unruhe*), which are marked phenomena in these cases. According to Stillé,§ the opium treatment was very serviceable in the disease as he observed it in Philadelphia. I have no personal experience to offer. I have no doubt, however, that the hypodermic injection of morphia is a remedy of great utility in this disease; but it should be used with the same caution which I have enjoined upon my readers as necessary in the treatment of acute mania.

In the psychical disorders *insomnia* is a prominent symptom, for the relief of which the morphia injection is especially indicated. When insomnia is the substantive disorder, a combination of morphia and atropia is better than morphia alone,—a fact which I shall develop in a future chapter.

In the treatment of **coup-de-soleil, sun-stroke,** very unexpected and gratifying results have been obtained

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* Reynolds's System of Medicine, vol. ii. p. 702.

† Die subcutanen Injectionen, op. cit. p. 31.

‡ Die hypodermatische Injection, op. cit. p. 156.

§ Epidemic Meningitis. Philadelphia, 1868.

by Dr. Hutchinson, at the Pennsylvania Hospital.* He injected one-fourth of a grain of the sulphate of morphia, which produced almost instant relief, and was followed by rapid recovery.

Hysteria.—In England Hunter,† in Germany Lander and Fronmüller,‡ were the first to employ the hypodermic method with morphia in the treatment of hysterical convulsions. Lorent§ recommends it in *hysterical melancholy.* In my own experience, no remedy has acted so promptly and satisfactorily in terminating a hysterical paroxysm as this. Five minims of my solution, or one-sixth of a grain of sulphate of morphia, is sufficient for this purpose.

Epilepsy.—Brown-Séquard was the first to indicate the utility of hypodermic injections of morphia in epilepsy. He combined with it atropia. Results as important as they were unexpected have followed this method. It has been found that not only are the paroxysms in violent cases quickly relieved, but permanent benefit has been obtained, by diminishing the number, frequency, and severity of succeeding attacks. This remedy disputes with the bromide of potassium for the first place in the amelioration and cure of epilepsy. One may succeed when the other fails; both, of course, fail frequently. It is important, then, to have clear notions as to the kind of cases in which one or the other should be preferred.

As has been pointed out by S. W. Duckworth Wil-

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* Pennsylvania Hospital Reports, vol. ii. p. 291.

† On the Speedy Relief of Pain, etc., l. c.

‡ Eulenberg, l. c. § Op. cit. p. 17.

liams,* Russell Reynolds,† and myself,‡ the bromide of potassium is most effective in cases of *grand mal* in which the paroxysms occur frequently, with great violence, and during the daytime, and less effective in those which occur chiefly at night. The bromide is most effective in epileptoid convulsions symptomatic of "coarse organic lesion" of the brain. It is less effective in the *petit mal* and in convulsive *tic*.

The hypodermic injection of morphia is preferable in epilepsy the paroxysms of which occur at night, in the *petit mal*, and in convulsive *tic*. It is not proper, as a general rule, in cases of epileptoid character dependent upon cerebral lesion.

When the paroxysms succeed each other rapidly and are violent, the injection may be made during an attack, and without loss of time. Ordinarily two or three times a week will suffice, and, whenever practicable, the onset of an expected attack should be anticipated. A very marked amelioration in obstinate cases may be thus induced. With the decline in number and violence of the seizures there will be witnessed, under this treatment, most gratifying improvement in the mental condition. For the treatment of epilepsy, seven or eight minims of my solution, or one-fourth of a grain, will be a sufficient quantity for each injection.

Scanzoni was the first to use the hypodermic injection of morphia in *eclampsia*. This practice was followed by Lander, Hermann, and Lehmann, with good

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* On the Bromide of Potassium in Epilepsy and Certain Psychical Affections. Pamphlet.

† The Practitioner, vol. i. p. 5.

‡ Fiske Fund Prize Essay. MSS.

results.* The injection is much safer than the inhalation of chloroform, almost as prompt in its effects, and quite as efficient in suspending the morbid reflex excitability. In the convulsions of infancy, whether dependent upon reflex irritation of teething, worms, indigestible food, etc., a medical friend, Dr. Henderson, of Covington, Kentucky, has found that the hypodermic injection of a small quantity (one-sixteenth of a grain) of sulphate of morphia will promptly terminate the paroxysms. This treatment must be conducted with caution in very young subjects. It will be prudent, in any case, to attempt relief by the ordinary measures, especially by the removal of the cause of irritation, before resorting to so powerful an agent. The dose for this purpose should not exceed one-sixteenth of a grain, and may be sufficiently powerful in one-half this quantity (one-thirty-second of a grain).

Chorea.—Hunter,† and Levick‡ of Philadelphia, employed the hypodermic injection of morphia in this disease with success. When the jactitations are incessant and violent, preventing sleep and causing injury to the soft parts, the patient wearing out at length, the use of the morphia subcutaneously has undoubted value. It is useful in those cases in which Trousseau§ was in the habit of prescribing enormous doses of morphia internally. But over ordinary cases of chorea, as Dr. Bristowe‖ has shown, "specific forms of treatment have little or no real influence," and suit-

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* Erlenmeyer, op. cit. p. 35.

† L. c. p. 27. ‡ American Journal of Med. Sciences.

§ Clinique Médicale de l'Hôtel Dieu, tome ii. p. 195–6.

‖ The Practitioner, No. X., April, 1869, p. 195.

able hygienic means will as certainly conduct the case to a favorable termination. Nevertheless, in the very violent cases to which I have referred there is no means of treatment equal to the hypodermic injection of morphia. Generally speaking, such cases require the maximum doses, as Trousseau's use of ten, twelve, and even fourteen grains of morphia daily with success sufficiently indicates. Commence with one-fourth of a grain, and increase according to the effect produced; it will rarely be necessary to exceed one grain at a single injection.

Tetanus and Hydrophobia.—Hunter used the hypodermic method in cases of traumatic tetanus, "giving sleep and diminishing the spasms," but without permanent relief, death ensuing in each. Ruppaner* injected two cases with the liq. opii comp., which very much assuaged the sufferings of the patients but did not retard the fatal termination. He urgently recommends further trials with this agent. More favorable results were obtained by others. Thus, Eulenberg† used it with success in a case of traumatic tetanus. Other cases have been reported, but the success of this method of using morphia cannot be considered encouraging. In idiopathic tetanus, and in trismus neonatorum, more favorable results have been obtained, but these forms of trismus are much more amenable to treatment than the traumatic. The subcutaneous use of the extract of Calabar bean, or of physostigmia, is, as I will show further on, much more effective in the treatment of tetanus.

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* Hypodermic Injections, p. 136.

† Op. cit. p. 136.

The sufferings of the patient affected with *hydrophobia* may be much diminished by the hypodermic injection of morphia, but I am aware of no case in which the fatal termination has been averted.

Local Muscular Cramp and Spasm.—Eulenberg has used the subcutaneous injection of morphia in the muscle spasm succeeding amputation of the thigh. I have obtained the greatest advantage from this method of treatment in the painful jactitations of the muscles which occur in cases of fracture. In a case of fracture of the femur on the paralyzed side of a hemiplegic patient, the injection procured instant relief to the very violent and persistent muscular spasms which occurred in a few hours after the injury. As is well known, Dr. Marshall Hall was the first to point out the fact that in paralysis of cerebral origin the muscular irritability is not lost. This fact is also admitted by Duchenne de Boulogne.* In the patient to whom I refer the muscular irritability existed in an exaggerated degree. Besides the pain which the violent spasm produced, union of the fractured femur would have been impossible if no means had existed for terminating the muscular spasms.

Neuralgia.—The greatest triumphs of the hypodermic method have been achieved in the treatment of neuralgia. As Dr. Anstie, in the able article already referred to, remarks, "The advantages of morphia, hypodermically administered, over opiate medication by the stomach, are such as would be *a priori* incredible, nor

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* De l'Électrisation Localisée, etc. Deux. édition, 1861, p. 338.

can they as yet be fully explained. In particular, it is impossible to account for the far greater *permanence* of its action in relieving nerve-pain, which is so marked as that its discovery has initiated quite a new era in the treatment of severe neuralgias."*

Following the classification of Valleix, the neuralgias are divisible into two classes:

I. Superficial Neuralgias.

II. Visceral Neuralgias.

The first class is subdivisible into the following:

Trifacial.

Cervico-occipital.

Cervico-brachial.

Intercostal.

Lumbo-abdominal.

Crural.

Sciatic.

The second class will be more conveniently referred to in connection with internal diseases.

It would be unprofitable to devote space to a special consideration of nerve-pain according to its anatomical seat, for the principles of treatment are the same. I purpose to make observations on the most important varieties to illustrate the hypodermic treatment in all.

Neuralgia of the fifth nerve, or trifacial, is the most important of the whole group. It occurs more frequently, is more painful, and is more difficult to cure. But from the lightest case of facial pain, due to irritation of decayed teeth or cold, up to the atrocious and

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* Op. cit.

incurable epileptiform tic, there are numerous gradations in respect to severity and curability.

In *toothache* the hypodermic injection of morphia is often immediately curative. It is, of course, less permanently beneficial when caries exists, but even in this case it affords great relief. It may also be used to diminish the pain of extraction. The facial neuralgia of pregnancy is promptly cured by it, as I have repeatedly ascertained by trial. This fact was first pointed out, I believe, by Dr. H. R. Storer, of Boston, the eminent gynæcologist of that city. These cases, as is well known, are extremely obstinate under the old methods of treatment, and those who have suffered from them on former occasions are exceedingly grateful for the relief so promptly and permanently afforded by the hypodermic method.

The attacks of neuralgic pain experienced in any portion of the distribution of the fifth are readily relieved by the same means. This remark is true of *migraine*, *hemicrania*, *clavus hystericus*, and other forms of neuralgic headache. I need hardly remind the reader that this method of treatment is not proper in that form of headache which often precedes, and is a symptom of, cerebral hemorrhage. That severe and obstinate neuralgia of the fifth, known as *tic douloureux*, is generally curable by the hypodermic injection of morphia, and if not curable, is always much ameliorated by this means. A single, or two or three injections may not suffice, but the persevering use of full doses may at length be successful. In obstinate cases the dose may be raised from one-fourth to one grain twice a day. Even that intractable form of tic

douloureux described by Trousseau* under the name "epileptiform neuralgia," may be much ameliorated by this means, and the existence of the patient elevated from a condition of abject misery to comparative comfort. The extent of the curative influence exerted by the hypodermic injection in cases of *tic douloureux* will depend upon the age of the patient, and upon the presence or absence of structural changes in the nerve, or in the brain. Certainly the injection, properly used, will render unnecessary those severe surgical measures sometimes practiced (section of the nerve) for temporary relief to the agony which the patient endures. I cannot too strongly insist that for decided relief of these severe cases very large doses are necessary—one grain twice a day. It is quite common to hear that hypodermic injections have been tried in a certain case and have failed, but upon inquiry it will be found that they have not been properly made, or that a sufficient quantity of morphia have not been used. In a case of severe epileptiform tic, now in my charge, a hypodermic injection had been used by another practitioner without avail, but in my hands a half grain of morphia does not fail to induce sound and refreshing sleep for the whole night, and great comfort and freedom from pain for some hours on the following day. What is equally gratifying in this case, the epileptiform convulsions have been rendered notably milder.

Cervico-occipital and *cervico-brachial neuralgia* are more amenable to treatment than tic douloureux.

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* Clinique Médicale, tome ii. p. 100, et seq.

A few injections of morphia will generally suffice to cure them.

I have had most gratifying success in the treatment of herpes zoster by this means. The hypodermic injection at once suspends the severe pain and burning (intercostal neuralgia) which accompany this disease, and cuts short the duration of the eruption.

Next to the severer forms of tic, the most troublesome neuralgic disorder with which we have to deal is *sciatica.* I may affirm with regard to this what Dr. Anstie has remarked about epileptiform tic, that the hypodermic method has inaugurated quite a new era in its remedial management.

In severe and protracted cases, in which changes in the nerve and in the nutrition of the limb have taken place, permanent relief cannot always be guaranteed to the patient, but the injections steadily continued in the maximum doses will, in a great majority of cases, effect a cure finally. When morphia fails, atropia may be tried, and *vice versa,* or both, as is preferable in my experience, may be employed together.

The other varieties of neuralgia call for no special comment. The principles of treatment are the same in all.

Notwithstanding the utility of hypodermic injections of morphia in the treatment of neuralgia, no judicious physician will rely upon them exclusively in the management of severe cases. Anæmia must be corrected by iron, cod-liver oil, the hypophosphites, etc. A suitable dietary and hygiene must be enforced. Meanwhile, if the pain is not permanently relieved by the injections, the existence of the patient

is rendered endurable while a proper remedial management is being pursued.

Is it necessary to confine the limits of the injections to the site of pain, or to the painful spots? I have already indicated my belief that the position of Mr. Chas. Hunter is, in the main, correct—that "localization" of the injection is unnecessary. But I admit the fact that exceptions exist.

Dr. Wood, the discoverer of the hypodermic method, Prof. Béhier, Erlenmeyer, Lorent, Eulenberg, and Messrs. Mitchell, Morehouse, and Keen,* think that better results follow injection into the painful spot. Dr. Anstie, although believing that remote injection is equally as effective in general, admits that exceptions are occasionally met with. Eulenberg bases his opinion on the fact that tactile and pain sensibility are diminished at the site of the injection.

For deep-seated neuralgias localization of the injection is impracticable. In superficial neuralgias, the nerve being readily accessible, it is comparatively easy to inject the fluid into the tissues surrounding the nerve. This practice is better than remote injection in cases of sciatica and of zoster, and in all cases of long standing in which the sheath or trunk of the nerve has become altered. When neuralgic pain is purely local, produced by alterations of nerve trunks, as for example many cases of sciatica, the injection of various irritants into the vicinity of the diseased nerve will often be followed by notable diminution of the pain, and sometimes by cure. This important fact

* American Journal of the Medical Sciences, July, 1865.

has been demonstrated by Luton,* Bertin,† and Ruppaner.‡ It is probably in this way that local injections sometimes succeed when remote injections fail.

Diseases of the Respiratory and Circulatory Systems.

There are certain neuroses of the respiratory tract which may be quickly relieved, if not cured, by the hypodermic method.

Laryngismus Stridulus.—Spasm of the muscles of the larynx, due to reflex irritation, is promptly relieved by the subcutaneous injection of morphia. In children, of course, a very minute quantity of morphia is necessary or proper. In adults a similar condition exists, due to pressure on the recurrent laryngeal nerves. In this case the relief is temporary, but for the time it is most striking. In *hysterical aphonia*, one injection will generally cure.

Cough.—That form of cough which is maintained by habit, and which so frequently succeeds to hooping-cough in adults, is quickly curable by this means. No method of treatment is so effective in hooping-cough as this, but with morphia, atropia should be conjoined, in order to secure the best results. In the cough of phthisis, as a palliative and to procure rest at night, the hypodermic injection is preferable to the internal use of morphia.

Asthma.—For the relief of an asthmatic paroxysm, there is no means now known comparable to the hypodermic injection of morphia or atropia. Prof. Sée,§

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* Archives Gén † Ibid.

‡ Hypodermic Injections, op. cit.

§ Practitioner, July, 1869, p. 1, et seq.

influenced by theoretical considerations, condemns the internal use of opium: "Opium," he says, "acts inversely to belladonna; it diminishes the frequency of breathing to the damage of the patient." He therefore recommends belladonna, a medicine styled by him "a vascular agent." Clinical experience is opposed to these theoretical views. I have ascertained that the hypodermic injection of morphia produces the following results in asthma:

It promptly relieves the paroxysm, enabling the patient to lie down and sleep.

It lengthens the interval between the attacks.

It renders succeeding paroxysms milder.

Ordinarily, I combine atropia with the morphia, in order to give large doses with safety; for in this disease, as in many other neuroses, the maximum doses are often required to accomplish relief. Prof. Hirtz has also found that the subcutaneous injection of morphia produces "marvelous results" in asthma. Although after an extensive use of this treatment, I cannot affirm that any cases have been cured, I can assert that, besides the immediate relief, permanent amelioration has been obtained in all submitted for any length of time to the treatment.

In any ordinary case of spasmodic asthma, five minims of my solution, or one-sixth of a grain, is a sufficient dose to commence with.

Catarrh.—In chronic catarrh, to moderate the cough, diminish expectoration, and to relieve the difficulty of breathing, the injection has been used with more or less advantage by Jarotzky and Zülzer.* I have used

* Erlenmeyer, op. cit. p. 40.

the injection, as a palliative, with much satisfaction in similar conditions.

Emphysema.—The hypodermic injection of morphia relieves the dyspnœa which attends emphysema as promptly as the asthmatic paroxysm. In this disease it has been used by Pletzer, Waldenburg, Kirkes, Jarotzky,* Lorent,† and others. It is merely palliative. In that spasmodic affection of the diaphragm, hiccough, which is sometimes obstinately persistent, the hypodermic injection affords prompt relief.

Pleuritis.—Nothing can be more satisfactory than the treatment of pleuritis by the hypodermic injection of morphia; the pain is immediately assuaged, and the morbid process arrested or diminished in violence. All therapeutists now admit the curative power of opium in cases of serous inflammation: this effect is much more decidedly manifest in the hypodermic than in the stomachic administration of this remedy. Pleurodynia, a neuralgia, is, of course, quickly terminated by the hypodermic injection.

In pleuritis the proper time for the hypodermic treatment is in the beginning, before effusion into the thoracic cavity has taken place.

Cardiac Neuroses.—I have had very satisfactory results from this method in the treatment of that form of *angina pectoris* which consists essentially in a neuralgic affection of the cardiac nerves. It is recommended by Bamberger‡ in the same disease, and is

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* Erlenmeyer, op. cit.

† Die hypodermatischen Inject., op. cit. ‡ Ibid.

approved by Erlenmeyer, Lorent, Eulenberg, and other authorities. In the "restraint neuroses" of the heart, a few cases of which have fallen under my observation, the very formidable symptoms were quickly removed by the morphia injection. Whether the symptoms are dependent on irritation of the pneumogastric, or reflex irritation through the sympathetic, the good effects of the injection are equally evident. As Handfield Jones* asserts, in which my own experience coincides, the inhibitory action on the heart is exerted very frequently through the gastric nerves. Other cardiac neuroses are those of rheumatic, malarial, and saturnine origin.† These agree as regards precordial pain, anxiety, breathlessness, and great depression of the heart's action, and are quickly relieved by the hypodermic injection of morphia. Of course, permanent relief will come of suitable treatment for the cachexia on which these neuroses are dependent.

Violent and irregular action of the heart, such as occurs in hysterical subjects, occasioning great anxiety and alarm, are at once relieved by a hypodermic injection of morphia. I have not observed any good effects from this treatment in cases of hypertrophy and semilunar disease, as suggested by Lorent. Violent palpitations occurring under these conditions, produced by mental emotion, reflex irritation, or other perturbating influences, may be palliated by this means; but my own observation is unfavorable to the use of hypodermic injections in cases of narrowing and obstruc-

* Functional Nervous Disorders. Am. ed., p. 215.

† Ibid., p. 218.

tion of the aortic orifice. I have, however, used it with advantage—morphia and atropia combined—in cases of dyspnœa dependent upon dilated right cavities, pulmonary œdema, and mitral disease.

Diseases of the Digestive Apparatus.

Whenever opium or the alkaloid morphia is indicated in any case of disease, and anorexia exists, the remedy should be administered by subcutaneous injection; such is the formulated expression of Dr. Anstie. Although morphia, when exhibited in suitable doses hypodermically, is much less apt to produce nausea and vomiting than when taken into the stomach, these unpleasant after-effects are not always absent after the former mode of administration. It is certainly true, however, that the hypodermic method does not nearly to the same extent interfere with digestion and assimilation.

Dyspepsia.—Dr. Clifford Allbutt,* of Leeds, England, is an enthusiastic advocate of the hypodermic injection of morphia in nervous dyspepsia with intolerance of food. I have myself seen cases in which the action of morphia was as happy as it proved in the hands of Dr. Allbutt. The relief which it affords is great in *gastralgia*. By allaying pain, arresting vomiting, and saving waste to the system at large, the hypodermic injection of morphia contributes powerfully to the cure of *gastric ulcer*. It is a remedy of the greatest value in the treatment of *acute gastritis*, quieting the viscus until the morbid process subsides, and

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* The Practitioner, vol. ii., 1869, p. 341.

obviating the necessity for the stomach administration of anodyne drugs.

One-fourth of a grain is a sufficient quantity to be injected daily in cases of dyspepsia, gastralgia, and ulcer. In acute gastritis, this quantity may be necessary every four or six hours. The site of the injection is of little consequence, but patients generally prefer the epigastric region.

Scirrhus.—In cases of *scirrhus* of any portion of the digestive tract, especially of the stomach, no palliative is comparable to the hypodermic injection of morphia. The existence of a patient afflicted with scirrhus of stomach is not only prolonged, but is rendered comparatively peaceful and calm, by this treatment, for it diminishes or arrests the vomiting, enables the food to be assimilated, gives freedom from pain, promotes sleep, and thus saves the strength.

Cholera.—The most instantaneous and striking relief is afforded by the hypodermic injection of morphia in *sporadic cholera.* It is indicated in this disorder after the irritant cause, whatever it may be, is evacuated from the intestinal canal. From one-sixth to one-half a grain, according to the severity and violence of the attack, may be injected into the epigastrium. The subcutaneous injection is strongly indicated in *epidemic* or *Asiatic cholera,* but I know of no case in which recovery was fairly attributable to this treatment. In this disease, the gastro-intestinal mucous membrane is not in a condition to appropriate remedies; hence the subcutaneous method is eminently rational; but morphia, it is agreed on all hands, must be used with caution.

The Vomiting of Pregnancy has been relieved by the hypodermic injection when all other means had failed. For the milder cases this treatment is unnecessary and improper; but in those severe cases in which life is reduced to the lowest ebb by the continual vomiting, and in which forced abortion has hitherto seemed the appropriate remedy, it is eminently successful. In all severe cases in which the ordinary remedies fail to give relief, recourse should be had to the hypodermic method. A daily morning injection ($\frac{1}{6}$ to $\frac{1}{4}$ grain), administered during the period of greatest difficulty, will enable gestation to proceed without danger to the mother, and without the necessity of adopting that serious alternative—abortion.

Colic.—In my practice I employ no other means of relieving the pain and spasm of colic. In most of these cases, of course, further treatment is necessary: constipation must be relieved; obstructions be overcome; the saturnine cachexia be removed; but the injection, by relieving spasm of the muscular layer of the bowel, permits these effects to be produced much more easily and speedily than would otherwise be possible. Cases of hepatic colic, within the range of my observation, have been quickly relieved by the hypodermic injection of morphia, where opium internally failed to produce the least mitigation of the pain, and where the inhalation of chloroform procured only the most temporary respite. When pain is very excessive, the reader should remember small doses may not suffice, but one-fourth and even one-half a grain may be necessary, repeated according to circumstances.

The same observations are applicable to *nephritic* and *uterine* colic.

Peritonitis.—Opium being the remedy *par excellence* for inflammation of serous membranes, the hypodermic injection of morphia should be employed in all cases in which promptness and completeness of effect may be desired. This is especially the case in peritonitis, whether primary or secondary. Moreover, as in many cases of this disease the alimentation is of prime importance, and as nausea and vomiting are frequently present, the stomach administration should be deprecated, and the hypodermic be preferred.

Neuralgia.—In the various forms of neuralgic pain which affect the abdominal organs, whether *gastralgia*, *enteralgia*, *hepatalgia*, *nephralgia*, etc., no remedy procures so prompt and, in many cases, complete relief as the hypodermic injection of morphia.

Constipation.—In many cases of colic due simply to constipation, the injection not only relieves the pain but overcomes the constipation. It is true that in many cases the first injection temporarily suspends the peristaltic movements, but when habitually used this effect disappears, and the normal movements are not diminished, but promoted. Cases in which constipation existed have thus been corrected during a course of hypodermic injections. A physiological fact which I have already noted, throws light upon this: in a few seconds after the injection borborygmi and distinct intestinal movements are observed. If, then, constipation exist in cases in which it may be desirable to use the hypodermic injection of morphia, this circumstance need not be considered a contraindication.

Diseases of the Genito-urinary Organs.

I have already indicated the utility of the hypodermic injection of morphia in nephralgia and nephritic colic. Lorent* refers to its use in parenchymatous nephritis, to relieve the headache of uræmic intoxication. My own experience is unfavorable to the use of hypodermic injections of morphia when the kidneys are seriously damaged.

Affections of the Bladder and Urethra.—In cases of chronic cystitis, I have given great relief by the hypodermic injection. It suspends those violent expulsive efforts which occasion the principal suffering. In *acute cystitis*, the injection, by procuring quiet to the organ, and by diminishing the irritability of the mucous membrane, will directly contribute to the cure. The sufferings of the patient afflicted with *calculus* may be thus prevented until operative measures can relieve him permanently. *Spasm of the bladder* is quickly relieved by the same means; as also that painful but obscure affection, "the bar," which sometimes succeeds too violent and prolonged sexual intercourse. The hypodermic injection may also be used to relieve *spasmodic stricture*, but for this purpose it is by no means equal, in my experience, to chloroform. It is convenient to blunt the sensibility preliminary to the operation of catheterism, and is a capital means for relieving *chordee*, and prolonged and teasing erections. But to prevent unpleasant erections and nocturnal losses,

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* Die hypodermatischen Injectionen, op. cit.

the use of morphia and atropia together is preferable to morphia alone. For information on this subject I refer the reader to the chapter on "Morphia and Atropia."

The hypodermic injection of morphia is capable of a variety of important uses in obstetric practice. It promptly arrests those *false and irregular pains* at the beginning of labor, which annoy the woman without advancing the case. In primipara, it has been used to diminish the sufferings of labor. It is much better than morphia, by the stomach, to procure rest and sleep during a prolonged first stage. No remedy is equal to the hypodermic injection of morphia for the relief of *after-pains*. In all of these circumstances no fear need be entertained that the judicious use of the injection will interfere with regular uterine contractions. The quantity to be administered will vary from one-sixth to one-fourth of a grain; the latter amount need rarely be exceeded.

The pain of *dysmenorrhœa* can be promptly relieved by subcutaneous injection of morphia; but for all pelvic pain, as Dr. Anstie has remarked, atropia is the best remedy. As a palliative in *scirrhus* of *the uterus* and of the *mammæ*, the hypodermic injection of morphia is much superior, in respect of economy and effectiveness, to the stomach administration of the same drug. Lastly, on this topic, in all cases of severe pain involving any of these organs the hypodermic injection of morphia is indicated.

Diseases of Constitutional or Specific Origin.—Dr. William Henry Fuller writes enthusiastically of the great value of the hypodermic injection of morphia for

relieving the pain of acute rheumatism. I shall have some remarks to make in a succeeding chapter upon the use of morphia and atropia in that disease, and will not now anticipate. I have used with great advantage the hypodermic injection of morphia to relieve the *nocturnal pains* of *tertiary syphilis.* Besides the complete and permanent relief to the pain which I have procured by persistence in the injections, I have observed, also, remarkable improvement in the lesions of bones and muscles. Not only in syphilitic, but other forms of disease in which pain precedes, and in which an altered condition of the nerves produces structural changes of tissue, I have observed that relief to the pain is followed by cessation of the morbid process in the part. This fact is well shown in zoster, an affection of the skin dependent upon some functional disturbance of its sensory nerves, which disappears very promptly after relief of the hyperæsthesia. Of course, in syphilitic neuralgia, the hypodermic injection should not be used to the exclusion of the iodide of potassium. In the cases in which I have employed it the pain persisted notwithstanding repeated use of large doses of the iodide—a condition of things not unfrequently encountered—for long use of this remedy, and to the point of saturation, to borrow a term from the chemists, induces a tolerance fatal to therapeutical efficiency.

In Certain Surgical Diseases and Operations.—To prevent shock, and to relieve pain after operations and injuries, the hypodermic injection of morphia is not as much used as it should be. No means affords such relief as this in the first few hours after *fracture* or

dislocation. The reduction of dislocations may be facilitated, and the pain prevented by the injection, in cases where it is undesirable or impracticable to use chloroform. It has recently been shown* that the *reduction of strangulated hernia* is much facilitated by the same means. In all operations requiring the knife, to prevent the after-pain, to sustain the vital powers, and to maintain the necessary quietude of wounded parts, the hypodermic injection of morphia should be used.

When it is desirable to prolong the stage of chloroform narcosis, one-sixth or one-fourth of a grain of morphia should be injected when the patient is anæsthetized. This has been ascertained to extend the anæsthesia for some hours longer, thus rendering prolonged inhalation the less necessary. A most important use of the injection is the prevention of the sickness and depression which follow chloroform inhalation in so many persons.

As a Physiological Antidote.—The subcutaneous injection of morphia may be used against the toxic effects of its physiological antagonists. The chief agents having this relation to morphia are the alkaloids of the family *Solanaceæ.* In a subsequent chapter, devoted to morphia and atropia, I will state the conclusions to which I have arrived in regard of the antagonism of these two agents.

The subcutaneous injection of morphia has been used against *strychnia poisoning*, but it is not so effective as physostigma. It has been used also against

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* The Practitioner, August, 1869.

poisoning by digitaline, but for this purpose it is inferior to atropia.

The Morphia Habit.—Before concluding this section it may be desirable to make some observations on the habit which is engendered by long-continued use of the subcutaneous injection of morphia, and the best method of avoiding the unpleasant sensations which appear when the injection is discontinued. As when morphia is administered for a lengthened period, by the stomach, so after long-continued hypodermic injection, the brain and nervous system become accustomed to the influence, and demand its repetition. If the injection have been administered at a regular hour for some time, the patient soon begins to experience characteristic nervous sensations as the time of the injection approaches; he becomes restless and "fidgety;" he is wakeful, and all his senses become acute; he experiences a feeling of vertigo and fullness of the head; nausea, and sometimes vomiting, occur. If the injections be suddenly suspended, much more serious disturbances become manifest: the patient lies awake at night, and is agitated with that terrible nervous sensation best expressed by the term "fidgets;" if sleep occur, it is short and fitful, and disturbed by horrible dreams and visions; during the day an inexpressible anxiety and restlessness is felt, rendering the patient unable to fix his mind on any subject, and making him the prey of the gloomiest apprehensions. He suffers from indigestion, nausea, and vomiting, and sometimes from diarrhœa; his appetite is poor, and the food, when eaten, lies heavily upon his stomach until ejected. Accompanying these symptoms there are observed

great muscular weakness and prostration, short and difficult breathing, rapid and tumultuous action of the heart. In extreme cases all of these symptoms exist in an exaggerated degree. The mental disturbance assumes a more prominent place; wakefulness, a suicidal tendency, hallucinations, and decided mental alienation may at last appear.

The degree in which these conditions will be produced by abrupt cessation of the injection will depend upon sex, constitutional peculiarities, length of time the habit has continued, and the *per diem* quantity which has been administered. They may be averted by judicious treatment. After quite a large experience in this method of treatment, I am able to say that I have not yet experienced any special difficulty in ceasing the injections after long use by following these rules:

Never stop the injections suddenly.

Diminish the dose very gradually, without the knowledge of the patient.

Never use morphia alone for a lengthened period, but with atropia.

As the morphia is diminished, increase the proportional quantity of atropia until the effects of the latter preponderate.

When the effects of the atropia are fully experienced the patient will generally begin to complain that the injection has lost its peculiar influence, has become unpleasant, and will desire that it be discontinued.

II.

ATROPIA.

The Solution.—The sulphate is the salt chiefly employed for hypodermic use. This supplies all the conditions: it is readily soluble in water; the solution is free from irritating qualities. The formula which I employ is the following:

℞.—Atropiæ sulphat. gr. ij;
Aquæ destil. ʒi. M.

Five minims of this solution represent one-forty-eighth of a grain. A much stronger solution may be used, as the following:

℞.—Atropiæ sulphat. gr. i;
Aquæ destil. ʒi. M.

A minim of this represents one-sixtieth of a grain. Or the following may be preferred:

℞.—Atropiæ sulphat. gr. i;
Aquæ destil. ʒij. M.

A minim of this contains one-one-hundred-and-twentieth of a grain. I prefer the first solution for these reasons:

It is sometimes desirable to inject very minute quantities in susceptible subjects, and this cannot be done when the solution is very concentrated.

The dose may be much more varied in a weak solution.

A *penicillum* develops very rapidly in an atropia solution, and at the expense of the atropia; the more concentrated the solution the greater the loss.

I have elsewhere stated the general objections to strong solutions, which apply to atropia.

On account of the rapid growth of the *penicillum*, the solution of atropia should not be kept too long, but should be prepared in small quantity frequently during warm weather. Filtration will, of course, free the solution from visible impurities, but considerable loss of strength will be noticeable each time.

Dose.—Extraordinary discrepancies are to be found in the statements of various authorities as to the quantity of atropia which may be used subcutaneously. Dr. Anstie* notes with surprise the large quantity advised by Trousseau—$\frac{1}{12}$ to $\frac{1}{6}$ of a grain—a quantity sufficient to produce most serious toxic symptoms. Dr. Ruppaner† gives the dose at $\frac{1}{60}$ to $\frac{1}{30}$ of a grain, Lorent‡ at $\frac{1}{250}$ of a grain, and Courty employed so much as $\frac{1}{6}$ of a grain at a single operation. Five minims of the solution which I recommend to the reader, or $\frac{1}{48}$ of a grain, is the largest amount desirable to use in most cases. Very great differences in

* The Practitioner, op. cit.

† Hypodermic Injections, op. cit.

‡ Die hypoder. Inject., l. c.

the susceptibility to the atropia influence are found to exist. Children bear a much larger proportional amount than adults. Women are much more susceptible than men. Persons having a light complexion are much more easily influenced by it than those having a dark complexion. A delicate female, having light blue eyes and flaxen hair, possesses, according to my observation, the maximum susceptibility. For such subjects two minims of my solution, or $\frac{1}{120}$ of a grain, is a sufficient dose to commence with, and even this amount may occasion severe symptoms. To produce a curative effect in many severe cases of neuralgia, *e.g.* sciatica, much larger doses than I have recommended may be necessary. It will rarely be required, however, to inject more than $\frac{1}{24}$ of a grain at one time.

PHYSIOLOGICAL EFFECTS.—The local symptoms at the point of puncture are the same as those I have described for morphia.

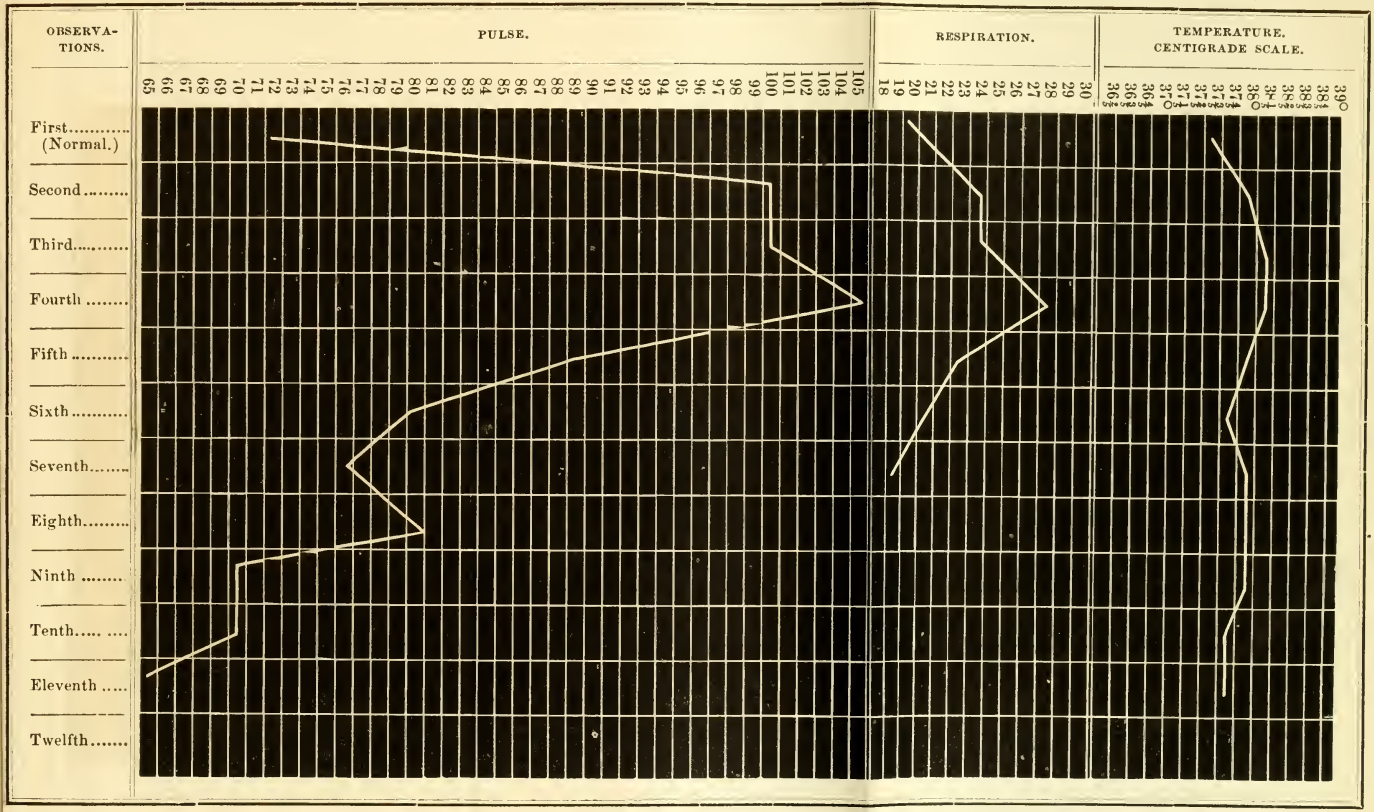
A peculiar dryness and pallor of the lower lip is the first systemic effect to be observed. The dryness quickly invades the mucous membrane of the mouth, fauces, and larynx, rendering deglutition somewhat difficult, and the voice husky. At the same time the pupil begins to dilate, reaching its maximum dilatation in about thirty minutes. With the dilatation of the pupil there occur also deranged accommodation—the vision being presbyopic—and dimness of vision, the outlines of objects being blurred and indistinct. Flushing of the face, more or less deep according to the temperament of the patient, fullness of the head with supraorbital pain and sense of distention, and giddiness, are now experienced. With the development of these effects

we observe increased action of the heart and rise in the bodily temperature. The pulse rises in a few minutes to nearly twice the normal number of beats, and the thermometer exhibits elevation of temperature; but the correspondence between pulse rate and temperature characteristic of fever does not exist. In the annexed diagram the influence of atropia upon the pulse and respiration movements, and upon the temperature, is exhibited.

At this period the subjective sensations of the patient, as well as the objective phenomena, are those of fever: the skin is hot and burning, and dry; the pulse full and bounding; the face flushed; the eyes injected; the head aches; the ears ring; the mouth is dry and hot; the voluntary movements are disordered in consequence of the vertigo and of the impairment of the muscular sensibility; objects appear confused, and distances cannot be correctly appreciated; hallucinations and illusions occur; when sleep takes place it is disturbed by vivid dreams, sometimes frightful, sometimes pleasing, the patient awaking and holding conversation with imaginary persons. Sometimes a somnambulistic state is produced, in which the patient walks about as if engaged in his usual avocations, talks with the objects of his visions, and quarrels and struggles with those who would oppose and restrain him.

Sometimes the face and forehead are of a vivid red hue, resembling in color the eruption of scarlatina; the fauces are also red and injected, and, to complete the resemblance to this eruptive fever, a whitish fur covers the tongue, through which the red and enlarged papillæ project.

Observations made every half-hour on Dr. De Courcey after the subcutaneous injection of one-forty-eighth of a grain of sulphate of atropia.



The dryness of the mouth, after some hours, is replaced by a moist condition, in which a viscid, sticky, and somewhat odorous secretion makes its appearance. Corresponding to this change in the mucous membrane of the mouth, some increase in the peristaltic movements of the intestines is to be observed, the evacuations being somewhat loose.

Frequent desire to evacuate the bladder is now experienced, with diminished power, the emission of urine taking place slowly, and with difficulty, and sometimes, indeed, only after repeated efforts does the flow occur.

The mental effects, generally such as I have described, are sometimes of a character to awaken grave anxiety. Great depression of mind, a melancholic state, with a suicidal tendency, at night horrible dreams and visions, leading to acts of violence, have been noted by me in some exceptional cases. I mention this so that the reader will ascertain what peculiar mental effects, if any, have followed the atropia injection, and avoid repeating it if the sensations above described have been experienced by the patient.

Such, in general, are the effects produced by the hypodermic injection of a full medicinal dose. These effects continue about twenty hours; the dilatation of the pupil, the disorders of vision, and the slowness and difficulty of micturition being the last symptoms to disappear.

Atropia cannot be considered very actively toxic. The symptoms which it produces afford ample warning of danger before the life of the individual is really placed in jeopardy. The sensations which accompany the full manifestations of its physiological effects are so

unpleasant that the patient early seeks relief, and the symptoms are so characteristic that a mistaken diagnosis is hardly possible.

When a fatal dose is received all of the effects which I have described exist in an exaggerated degree. The pulse finally becomes small and thready, the action of the heart weak, and coldness of the surface succeeds to the unnatural warmth. This change in the symptoms indicates that the "irritability" of the organic muscular fiber is exhausted.

In order to a thorough comprehension of its therapeutical action, we must form some exact notions of the mode in which these physiological effects are produced.*

The facts to be investigated are these:

The dilatation of the pupil.

The dryness of the mouth (arrest of secretion).

The increased action of the heart and lungs.

The rise of body-heat.

The influence on sensibility and motility.

Several opinions have prevailed as to the mechanism by which the dilatation of the pupil is accomplished.

This act, as well as the presbyopia, is now known to be produced through the influence of atropia on the organic muscular fiber. By contraction of the radiating fibers of the iris, which are innervated by the sympathetic, the pupil dilates; by a similar action on the muscle of accommodation, the lens is elongated, its

* I have examined this whole question in my Prize Essay of the National Medical Association for 1869, on Atropia, its Physiological Effects and Therapeutical Uses, to which the reader is referred for full information.

diameter diminished, and the subject becomes presbyopic. It is probable, also, that this effect is facilitated by the paralyzing action of atropia on the oculo-motor nerve.

A number of experiments have been made to determine the character of the influence exerted by atropia upon the heart and lungs. The part that paralysis of the pneumogastric plays, the part that direct stimulation of the cardiac portion of the sympathetic takes in the production of the phenomena, have been earnestly discussed. The inhibiting influence of the pneumogastric on the action of the heart is well understood: if the terminal filaments of this nerve are paralyzed the action of the heart increases. It has been found, however, by Lemattre,* that the action of the heart is increased by atropia, notwithstanding division of the pneumogastric; this agent must, therefore, exert an immediate stimulant action on the cardiac ganglia of the sympathetic. This same effect is witnessed on the organic muscular fiber of the arterioles, as demonstrated by Lemattre in the vessels of the frog's foot, and confirmed by myself. I have demonstrated another fact: the contraction of the vessels after a time ceases, and relaxation takes place. This change is coincident with a weakened action of the heart; in other words, the atropia finally exhausts the irritability of the organic muscular fiber. This is a capital fact, which must not be forgotten in our therapeutical employment of atropia.

The rise in body-heat is a product of increased oxidation due to the greater activity of the circulation.

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* Archives Générales, 1864.

The redness of the skin and mucous membrane is due to the larger amount of blood pumped into the capillaries, and the increased arterial tension. The increased oxidation finds expression in a much greater excretion of urea and the urates.

There are several physiological facts which explain the action of atropia in arresting secretion of the pulmonary and intestinal mucous membrane. Prevost* has demonstrated that ablation of the spheno-palatine ganglion is followed by greatly increased secretion from the Schneiderian mucous membrane. The action which atropia exerts on the ganglia of the sympathetic must be the opposite of this.

Patients brought fully under the influence of atropia generally experience considerable disorder of voluntary movement. This effect is compounded of vertigo, diminished sensibility of the sensory nerves, and loss of co-ordinating power. The exact relation of these phenomena may be easily demonstrated on frogs and certain warm-blooded animals. The reader who desires full information on this topic will find in my Prize Essay, already referred to, an analysis of the observations of Botkin of St. Petersburg, Lemattre, Harley, Fuller, and others, and numerous experiments of my own.

THERAPY.—It will be convenient to arrange the subjects under this head in the same way as in the section on the therapeutical applications of morphia.

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* Archives de Physiologie Normale et Pathologique, vol. i.

Diseases of the Brain and Nervous System.

Cerebral Diseases.—The subcutaneous injection of atropia is contraindicated in inflammatory affections of the brain and meninges, for a constant result of the toxic effect of this remedy is hyperæmia of these organs. I have seemed to produce some good results, and certainly have relieved the referred pains of the extremities, in cases of general paralysis. The "*late rigidity*" which comes on in many cases of hemiplegia, and which is often accompanied by severe pain in the affected limbs, has been much benefited by the hypodermic injection of atropia. The pains of *progressive locomotor ataxia* and that annoying disturbance of the sensory nerves, "*the fidgets*," which so constantly attends upon this disorder, may be relieved by this means. It has seemed to me that the subcutaneous injection of atropia exercised some influence, also, in retarding the progress of this disorder. Lorent has used the injection of atropia with advantage for relieving the pains which accompany *chronic meningitis* and *myelitis*. According to the views of Brown-Séquard, who holds that belladonna, by producing contraction of the arterioles, diminishes the supply of blood to the cord, the hypodermic injection of atropia ought to be very serviceable in myelitis. But it is now known that the increased action of the heart, and the greater arterial tension produced by atropia, favor hyperæmia of these parts.

The hypodermic injection of atropia is serviceable in certain cases of *delirium tremens*. The indications for its use are these:

Obstinate insomnia, with great restlessness.

Weakened action of the heart; coldness of the surface; clammy sweat.

Failure of nutrients, bromide of potassium and hypodermic injections of morphia, to quiet the delirium and induce sleep.

In similar conditions in the *psychical disorders* the subcutaneous injection of atropia is serviceable. This method of treating these disorders has the sanction of the eminent authority of Graefe. My own observation entitles me to insist on this caution: the use of atropia is unsuited to cases in which there is hyperæmia of the nervous centers, or in cases of excitement with power. Moreover, it is not suited to cases of melancholia, for the reason, already stated, that in many persons it produces great despondency of mind.

Atropia cannot be considered a *hypnotic* in the true sense of that term. It is sometimes said to produce this effect indirectly; by allaying pain, it is believed to render sleep possible. This, in the opinion of the author, is not a correct statement of the ground of its utility in certain cases. It is sometimes very useful as a hypnotic in cases of wakefulness and coma-vigil, dependent upon cerebral anæmia.

Neuralgia.—The subcutaneous injection of atropia is not as effective in the treatment of the neuralgias in general as morphia by the same method. The systemic effects of atropia are also more unpleasant. For these reasons morphia is generally preferred. Nevertheless, when morphia fails to produce the desired result, or disagrees with the patient, as is sometimes the

case, atropia may be used. In certain neuralgias, it must be admitted also, atropia is to be preferred to morphia, *e.g.* in pelvic pain, in which Dr. Anstie considers it superior to morphia, in sciatica, and in certain cases of *tic douloureux*. In the pain of the various forms of *dysmenorrhœa*, in *ovarian neuralgia*, and in the pelvic pain experienced a few days after delivery, and due to the pressure of the womb on certain nerves, atropia by subcutaneous injection is most serviceable.

The principal triumphs of atropia over neuralgia have been in cases of *sciatica*. It is now universally admitted that atropia is the best remedy for this disease. First proposed and used by Mr. Hunter, it was afterward employed by Béhier, Courty, Oppolzer, Lorent, and others. It has been found, however, that distant injection, and even injection into the subcutaneous tissue of the affected thigh, do not produce such good results as throwing the fluid deeply into the neighborhood of the affected nerve. More frequently, indeed, than in any other form of neuralgia, except the most obstinate and protracted cases of tic douloureux, the nerve itself, or its sheath, has undergone structural alteration; the limb is often diminished in size, its temperature and sensibility lowered, and the power of its muscles impaired. Under these circumstances, more advantage is to be derived from local than from distant injection, just as Luton, Bertin, and Ruppaner have cured such cases by the injection of irritants into the affected parts.

In severe cases of sciatica and tic douloureux one-twenty-fifth of a grain of sulphate of atropia may be

injected; but it should not be forgotten that this quantity will excite very severe symptoms in susceptible subjects. Generally, five minims of my solution, or one-forty-eighth of a grain, will produce decided atropinism. Cessation of the pain is not immediate upon the systemic effects, as Mr. Hunter originally pointed out; indeed, the pain is often at first increased, but improvement takes place after a variable interval, and is often more permanent than after the morphia injection.

Tetanus and Hydrophobia.—In tetanus, atropia has been used in numerous cases, but without success. Recovery has undoubtedly occurred in certain chronic cases, and in idiopathic tetanus; but it does not appear that the result was fairly attributable to the subcutaneous injection of atropia. Within the sphere of my observation, it has been freely used in cases of tetanus and hydrophobia, but without permanent benefit.

Epilepsy.—Brown-Séquard proposed the subcutaneous use of atropia in epilepsy, but he combined it with morphia. Erlenmeyer used it, but with a negative result. My own experience with atropia in this disease is as combined with morphia. The subcutaneous injection of atropia may be employed, instead of the internal use of belladonna, on the method of Trousseau;* but there are other plans of treatment superior to this.

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* Clinique Médicale, tome ii.

Diseases of the Respiratory and Circulatory Organs.

The subcutaneous injection of atropia is applicable to the treatment of certain neuroses of the thoracic viscera.

Asthma.—Courty was the first to employ atropia subcutaneously for the relief of asthma. He injected the solution over the pneumogastric nerve. Belladonna, in large doses, is now held to be the best remedy by Hyde Salter, Prof. Sée, and others.* The latter recommends belladonna because it is a "vascular and cardiac" agent, and "because the means of modifying respiration is to be found in the power to alter the pulmonary circulation." The hypodermic injection of atropia is preferable to the internal use of belladonna for the following reasons :

The effect is more speedy and certain.

The relief which it affords is greater and more lasting.

In my experience cases of emphysema and spasmodic breathing, due to dilatation of the right cavities of the heart, are not so much benefited by atropia as asthma. I think it prudent to add a caution here: as atropia exhausts the irritability of the sympathetic ganglia, it is not proper to push the use of this agent in cases in which the muscular tissue of the heart is weakened by dilatation or fatty degeneration.

In order to procure the greatest relief to the asthmatic paroxysm, the injection should be made promptly at the beginning of the attack. The dose will vary from

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* The Practitioner, July, 1869.

$\frac{1}{96}$ to $\frac{1}{48}$ of a grain. It may be inserted at any convenient situation. Succeeding attacks should be anticipated if possible, the injection being made when the first warnings are felt by the patient. As the effect of the atropine injection reaches its maximum in about a half-hour it will at this time be perceived whether a sufficient quantity have been administered.

This method of administering belladonna is much to be preferred to the stomach administration, or to the methods of fumigation, pulverization, or inhalation, notwithstanding fumigation is strongly urged by Prof. Sée* in a late utterance on the subject of asthma.

Harley†—influenced by the fact that great increase of the heart's action follows the administration of atropia, a fact, indeed, previously much insisted on by V. Bezold—recommends this agent as a cardiac stimulant in conditions of great depression of this organ. It is certainly exceedingly useful in those restraint neuroses in which the inhibitive action is exerted through the pneumogastric, for by paralyzing the terminal filaments of this nerve and stimulating the cardiac ganglia of the sympathetic, the action of the heart is quickly improved and the depression overcome. It is in this action, according to Prof. Sée, that we have an explanation of the utility of atropia in asthma.

Diseases of the Digestive Apparatus.

Atropia, it will be remembered, first arrests secretions of the intestinal mucous membrane, but in the reaction

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* Bulletin Générale de Thérapeutique, 15 Août, 1869.

† Gulstonian Lectures, also Vegetable Neurotics.

which ensues from this state, increased secretion takes place. It promotes peristaltic movements by its action on the circular fibers of the intestinal tube.

Vomiting.—Sea-sickness and the vomiting of pregnancy are both relieved by subcutaneous injection of a small quantity—$\frac{1}{120}$ of a grain of atropia. It may be inserted over the epigastrium.

Colic.—The various forms of colic may be relieved by this agent, but it is not so effective in most of them as morphia. It is adapted to cases of colic dependent upon constipation or upon lead poisoning, but the most desirable results are obtained by the conjoined administration of morphia and atropia.

Diseases of the Urinary and Genital Organs.

For all varieties of pelvic pain, as Dr. Anstie has informed us, the subcutaneous injection of atropia is the best agent. I need not repeat here what has already been said on this topic.

Bladder Diseases.—In *dysuria* and *enuresis* it is often most effectual. Belladonna has long had a deserved pre-eminence in the treatment of nocturnal incontinence of urine. Atropia by subcutaneous injection is the most effective way of administering it.

Irritation of the bladder, when arising from a nervous erythism, may be relieved in the same way. That troublesome disorder—*spermatorrhœa*—is most successfully treated by the hypodermic injection of atropia. Two indications are to be supplied in many of these cases: the erotic sensations which originate during the sleeping state are to be suppressed; the reflex act of emission to be prevented. No agent accomplishes this

more successfully than the subcutaneous injection of atropia at bedtime and at such intervals as observation has shown to be necessary.

Constitutional Diseases.

Remarkable relief to the pain and soreness of *acute rheumatism* has been obtained by Lorent from the subcutaneous injection of atropia. This treatment has been suggested by Harley as if it were an original idea with himself. He recommends that the atropia be injected in the neighborhood of the inflamed joint. I have followed this practice with great relief to the patient. One injection of $\frac{1}{48}$ of a grain daily will generally be sufficient to quiet the pain; but morphia may be combined with it advantageously, if the patient be wakeful. It has seemed to me to exercise no little influence over the severity and duration of the disorder.

As a Physiological Antagonist.—The subject of the antagonism of morphia and atropia will be discussed in the next chapter.

The subcutaneous injection of atropia may be used against the toxic symptoms of certain vascular agents, as aconite, veratrum viride, tartar emetic, digitalis, which produce great depression of the heart's action. It has been proposed, also, on insufficient grounds, for relief of poisoning by hydrocyanic acid. In my prize essay on atropia I have shown that hydrocyanic acid in toxic doses acts too speedily for atropia to influence the result, and that animals fully under the effects of atropia are quickly poisoned by an ordinary toxic dose of the acid.

III.

MORPHIA AND ATROPIA.

The Solution.—I have recommended the practitioner to keep prepared, in his hypodermic case, solutions of morphia and atropia made according to formulas already given. At the time of administration they may be mixed in proportions adapted to the indication in each particular case. For many purposes the following solution may be used:

℞.—Morphiæ sulph. gr. xvi;
Atropiæ sulph. gr. i;
Aquæ destil. ℥i.
M. Filter.

Five minims of this solution represent one-sixth of a grain of morphia and one-ninety-sixth of a grain of atropia. A better proportion is one-fourth of a grain of morphia, and one-ninety-sixth of atropia, or, as follows:

Morphia solution, 8 parts;
Atropia solution, 2 parts.

For reasons which will presently be stated, one-twenty-fourth of a grain of atropia is considered equivalent, in toxic power, to one grain of morphia.

The relative dose of these agents, when mixed, will depend upon the character of the case for which they are administered.

When the object is to relieve severe neuralgias which resist ordinary doses, the maximum quantity is required. By combining atropia with the morphia, we can inject a quantity of the latter agent which it would be very unsafe to use alone. Thus $\frac{1}{2}$ and even 1 grain of morphia and $\frac{1}{48}$ and $\frac{1}{24}$ of a grain of atropia may be injected together, relying for immunity against ill effects, upon the antagonisms existing between them.

Physiological Effects.—Although much has been said in the preceding pages upon the physiological effects of morphia and atropia, when separately administered, it is necessary now to show the influence which they reciprocally exert when administered together. Their so-called "physiological antagonism" may be most conspicuously exhibited by a comparison of their individual with their combined action on the different parts of the body.

1. *On the Nervous System.*—Both act upon the brain—atropia producing delirium, hallucinations, and disturbed sleep; morphia causing, generally, somnolence. Both relieve pain, but this effect is much more decidedly the property of morphia. Both produce disorders of motility, staggering, difficulty of co-ordinating muscular movements, vertigo, confusion of mind, and headache. When given together, these effects are curiously modified.

Morphia corrects the hallucinations and phantasms of atropia.

Atropia in small doses—$\frac{1}{96}$ of a grain—increases the hypnotic power of morphia; but if the quantity of atropia be sufficient, it overpowers the effects of mor-

phia on the cerebrum, causing wakefulness or disturbed sleep, phantasms, and illusions.

The pain-relieving power of morphia is increased by atropia.

The disorders of motility, and the vertigo, are not diminished when the two agents are used together, but the after-headache and confusion of mind are much less.

When toxic doses are used, the narcotism of morphia is overcome by atropia, and *vice versa.* In a case which occurred to myself, and which I have already referred to, serious symptoms produced by 1 grain of morphia were relieved by $\frac{1}{24}$ of a grain of atropia. As, however, the effects of atropia are much more prolonged than morphia, it is not easy to exactly counterbalance the effects of one by the other. The cases of morphia poisoning, in which atropia was used as an antidote, that have fallen under my observation, received too much atropia, the toxic symptoms of the latter remaining long after the narcotism of the morphia had disappeared.

Upon the organic nervous system these agents seem exactly to antagonize each other.

Morphia produces contraction of the pupil, and a tetanic condition, according to Graefe, of the muscle of accommodation; atropia produces dilatation of the pupil, and contraction of the ciliary muscle. When used together, these effects may be precisely balanced. It takes, however, but a minute quantity of atropia to overcome the action of morphia on the pupil. When these effects on the pupil are balanced, it does not follow that the muscle of accommodation is in a con-

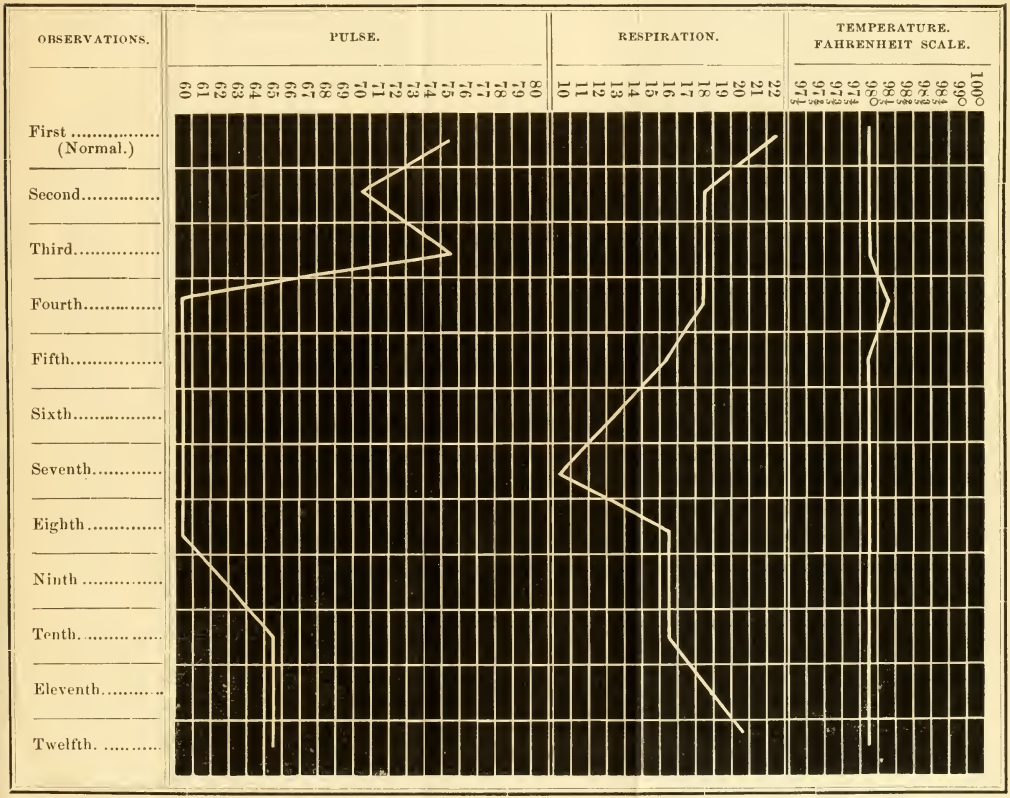
dition to act in a normal manner, for visual defects frequently remain.

Morphia and atropia antagonize each other's action on organic muscular fiber. Morphia prevents the contraction of the arterioles produced by atropia, and, as a consequence of this action, prevents the subsequent relaxation of the muscular fiber. They antagonize each other, therefore, as respects their action on the arterial tension.

2. *On Circulation and Respiration.*—Morphia depresses the action of the heart; atropia is a powerful cardiac stimulant. Morphia produces pallor of the surface, and reduces the external temperature; atropia causes redness and injection of the skin and elevation of the body-heat. The extent to which they modify each other's action is well exhibited in the annexed diagram. It will be seen that the antagonism between them does not extend to the respiratory function; for, whilst morphia administered alone depressed the respiration from 17 to 12 per minute, morphia and atropia combined reduced the number from 18 to 10. When Dr. De Courcey received the morphia alone, he experienced much less soporific effect than when both agents were injected together; and to this quiescent state of the cerebral functions is to be attributed the slower respiratory movements. The morphia exercises a marked influence over the increase of body-heat produced by atropia. Notwithstanding this, the flushing of the face and the strong subjective sense of heat are experienced by the patient almost as fully when morphia is administered with atropia, as when atropia is given alone.

In the experiment represented on the diagram, the

Observations made every half-hour on Dr. De Courcey after the subcutaneous injection of one-quarter of a grain of sulphate of morphia and one-ninety-sixth of a grain of sulphate of atropia.



quantity of atropia was not sufficient to produce the full degree of antagonism, otherwise the pulse line would have continued on the same plane. In so far as the atropia influence preponderates, a progressive rise in the pulse rate is noted.

3. *On the Digestive Apparatus.*—As regards dryness of the mucous membrane of the mouth, fauces, larynx, etc., there is no antagonism, but both agents produce this state and exalt it when administered together. Morphia tends to produce constipation; atropia relaxes the bowels. When administered together, they produce, almost immediately, intestinal movements; frequently borborygmi, and sometimes sharp pain, and the bowels are kept in a soluble state. The sickness and nausea, and the not uncommon great depression of the vital powers caused by morphia, are opposed by atropia. These agents may therefore be given together in cases in which morphia cannot be borne alone. The after stomachal effects of morphia—indigestion, loss of appetite, a pasty tongue—are much diminished by the atropia, but are not absolutely prevented. Atropia itself is capable of producing these stomach disorders when used in considerable doses; hence, to produce the result which I have described, the proportion of morphia and atropia should be as follows:

Morphia, one-fourth of a grain;

Atropia, one-ninety-sixth of a grain.

4. *On the Genito-urinary Organs.*—These agents are antagonistic as to their effects on the kidneys and the urinary excretion. Morphia suspends, and atropia promotes, the functional activity of the kidneys. By inducing congestion of the Malpighian tufts, and in-

creasing the *vis a tergo*, atropia acts as a diuretic, and with the additional water there strains off from the blood the larger amount of urates produced in the more rapid metamorphosis of tissue. Morphia increases the action of the sudoriparous glands, and atropia diminishes it, thereby in the one case lowering, in the other case exalting, the functional activity of the kidneys.

Both produce dysuria, but this result comes of a different action in each case. Morphia impairs the contractile power of the muscular coat of the bladder, so that it contracts with difficulty, the emission of urine taking place slowly; atropia maintains steady tonic contraction of the sphincter, so that it dilates slowly under the voluntary effort, when the desire to micturate is experienced.

Morphia impairs but slightly, atropia to a considerable extent, the sexual appetite; both diminish the ejaculatory effort.

THERAPY.—It would be a waste of space to repeat the therapeutical applications of morphia and atropia already given with considerable fullness in the preceding sections. Nevertheless, it is necessary to indicate the circumstances requiring or permitting their conjoined administration. A general rule may be formulated as follows:

Whenever the hypodermic injection of morphia is proper and necessary, atropia should be combined with it, unless contraindicated.

In the *psychical disorders*, in which power is in excess, the conjunctivæ injected, the temperature high, morphia should be used alone. When power is deficient, the tendency being to depression, atropia should

be combined with it. This is the rule, also, for other *affections of the brain* in which the subcutaneous injection is indicated.

For the relief of *insomnia*, or to procure sleep, the combination of morphia and atropia is to be preferred. The reader should not forget that an excess of atropia, or an amount of atropia sufficient to antagonize the cerebral effects of the morphia, will prevent sleep. They should be used in the proportion of $\frac{1}{120}$ to $\frac{1}{96}$ of atropia to $\frac{1}{4}$ grain or $\frac{1}{2}$ grain of morphia. As the susceptibility to atropia varies immensely, the precise quantity to be employed in any case must be regulated accordingly.

In the treatment hypodermically of the *various convulsive disorders*, morphia and atropia should be combined.

The *neuralgias* are best treated by the combined morphia and atropia solution. There are several reasons for this:

Much larger doses of morphia may in this way be injected without danger to the patient, and the larger the quantity, as Brown-Séquard has shown, the greater the curative power.

Morphia and atropia combined are more effective than either singly.

The systemic effects during the time of maximum narcosis, and also after the narcosis has disappeared, are much less unpleasant and depressing when the two agents are combined than when morphia is used alone.

Sometimes atropia is better borne than morphia, and *vice versa:* in this case the agent whose effects are least unpleasant should be in excess.

In *sciatica* atropia is often more effective than morphia: the proportions in which they should be used are as follows: $\frac{1}{24}$ of a grain of atropia, $\frac{1}{2}$ grain of morphia: here the physiological effects of atropia predominate, but the toxic effects are guarded by the morphia.

In *neuroses of the respiratory and circulatory organs*, morphia and atropia should be used together. This is especially the case in *angina pectoris* and *asthma*, with the caution I have already given as to the use of atropia in certain diseases of the heart. Morphia alone is to be preferred in *pleuritis*.

In the *diseases of the digestive apparatus*, requiring hypodermic medication, morphia and atropia should be used together.

As a general rule, in *diseases of the urinary and genital organs*, the two agents should be combined. For some purposes atropia should be in excess, as in *spermatorrhœa*, when the more decided anaphrodisiac effect of this agent is indicated. In cases of *pelvic* and *uterine pain*, atropia should be proportionally in larger amount than morphia.

Acute rheumatism, *rheumatic gout*, *muscular rheumatism*, and *myalgia* are best relieved by a combination of morphia and atropia, the latter being in excess, as respects its physiological action, of the former. The injection of atropia, thus guarded by morphia, exerts in these diseases an action beyond the relief of pain, how desirable, soever, that may be: it modifies in a way not now understood the morbid process. The progress of research renders it more and more probable that rheumatism is an expression of disorder in the nervous

system, rather than an affection *per se* of the fibrous structures. Besides relieving in some way this centric disturbance, atropia favors the excretion from the blood of products (the urates) representing the active but imperfect tissue change occurring in these diseases.

In surgical disorders of various kinds, the combined use of morphia and atropia has most important and varied applications: *to prevent and relieve shock; to cure pain; to relax spasm; to facilitate surgical operations.* Whenever, in surgical practice, the hypodermic injection of morphia and atropia is indicated, the following rule should regulate the relative proportion in which they are employed:

If the action of the heart be feeble, the surface cold, and the vital powers depressed, atropia should be in excess as respects the physiological effects.

Treatment of Toxic Symptoms caused by Morphia or Atropia.—I may assume, notwithstanding the objections of Harley and the results of experiments on animals by Brown-Séquard, that the physiological antagonism of morphia and atropia has been amply demonstrated by cases of poisoning occurring in man.

In treating cases, the difficulty of precisely regulating the amount necessary to overcome the toxic symptoms is not easily surmountable. I ascertained, in the case which occurred to myself, that one-twenty-fourth of a grain of atropia was equal in toxic power to one grain of morphia. The state of the pupil affords valuable, but not unerring indications; atropia possesses more power, relatively, over the movements of the iris than morphia.

In a case of morphia poisoning, subcutaneous injection of atropia should produce the following results:

Dilatation of the pupil.

Flushing of the face succeeding to pallor.

Dryness and warmth of the skin succeeding to a cold and clammy sweat.

Rise in the pulse rate and temperature.

Return of reflex movements of eyelids and fauces.

The dilatation of the pupil should be slightly maintained, and should not be carried to the exaggerated degree sometimes thought necessary. The mistake should not be made of confounding the sopor produced by morphia and atropia with morphia coma. This caution is the more necessary because this sleep is often considered a condition of danger requiring renewed administration of the antidote, and the patient is at length poisoned by atropia.

Atropia, relatively considered, does not equal morphia in toxic activity. Severe physiological effects do not necessarily imply a condition in which life is endangered. It is to be remembered that the toxic effects of atropia endure much longer than those of morphia, and hence repeated applications of the physiological antidote may be required.

IV.

STRYCHNIA.

The Solution.—A solution for hypodermic use may be prepared as follows:

℞.—Strychniæ sulphat. gr. ij;
Aquæ destil. ℥i. M.

To obtain a perfect solution, heat in a test-tube until all the crystals disappear; or the crystals may be triturated in a mortar and the distilled water added gradually. Five minims of this solution represent one-forty-eighth of a grain. Eulenberg proposes the following formula:

℞.—Strychniæ sulphat. gr. ij;
Aquæ destil. ʒij. M.

One minim of this contains one-sixtieth of a grain. The sulphate of strychnia, as found in the shops in this country, is not so soluble as this formula indicates. Solution in this proportion may be effected by the aid of heat, but on cooling the salt will be deposited. Even when it is dissolved in the proportion I have recommended (gr. ij–℥i), after a time crystals will slowly separate and adhere to the glass. For this reason, a solution long kept is unfit for use.

The solutions of strychnia, much less than the other alkaloids, are spoiled by the development of a *penicillum*, but this takes place only after long standing and exposure to the air.

Dose.—As is the case with other alkaloids, authorities differ very much as to the quantity of strychnia proper for a hypodermic injection. Lorent employed from $\frac{1}{25}$ to $\frac{1}{10}$ of a grain of nitrate and muriate. Courty and Eulenberg have used so much as $\frac{1}{8}$ of a grain at a dose. These large doses are apt to produce trismus and opisthotonos. The doses used by Hunter varied from $\frac{1}{90}$ to $\frac{1}{24}$ of a grain. Dr. Echeverria, of New York, injected, in the cases of paralysis treated by him, $\frac{1}{60}$ to $\frac{1}{30}$ of a grain—the latter dose producing in the patient, a boy, toxic symptoms. I have injected $\frac{1}{24}$ of a grain. This has seemed to me the maximum quantity which can be used with a proper regard to the safety of the patient. Generally in adults I inject 5 minims of my solution, or $\frac{1}{48}$ of a grain.

Physiological Effects.—When injected under the skin, a sensation of heat and smarting persists for some time in the part. The skin also becomes red in the neighborhood of the puncture; a subjective sensation of warmth is perceived in the limb, and an actual rise in temperature may be noted. At the same time erection of the hair-follicles (*cutis anserina*) takes place.

In a few seconds pain or distention is felt in the abdomen, intestinal movements and loud borborygmi occur, just as is the case so frequently after the hypodermic injection of the narcotic alkaloids. Next the pupils dilate, deep-seated pain and throbbing are

felt in the brain, and an unpleasant giddiness renders the erect posture painful, and standing or walking uncertain. Ringing in the ears, detonation and anxiety, a feeling of dread and flashes of light before the eyes, are also quite commonly experienced. The countenance of the patient affords some indication of the cerebral disturbance, appearing anxious and distressed.

The foregoing symptoms are more severe if larger doses be administered, and in addition there occur some stiffness of the jaws, jerking of the extensor muscles, and sharp pains like electric shocks shooting through the limbs. Dr. Echeverria has so well described the toxic symptoms that I transcribe his account. My own observations supply no further experiences than those I have just detailed.

"I injected first the right thigh, and about two minutes after, the left. In two minutes more the boy commenced to sigh, and to have a meaningless smile, with stiffness in the jaws, soon passing into real trismus. The pupils were largely dilated, the face congested, and tetanic spasms of the respiratory and cervical muscles followed. Every attempt to articulate a word awoke a spasm. He could neither speak nor be touched without being seized with a jerk, and the whole surface of the body was in a perspiration."* In another case Dr. Echeverria had similar experiences. He thus describes them: "In about eight minutes she complained of giddiness, and was soon seized with trismus and

* Treatment of Paralysis by Hypodermic Injections of Strychnine. Medical Communications of the Connecticut State Medical Society, 1868.

opisthotonos. The tetanic spasms were not violent and were accompanied by general perspiration, congestion of the face, and enlargement of the pupil." Other important observations were made by Dr. Echeverria. "The temperature of the limbs was always raised after the injection. The frequency of the pulse was also augmented. The capillary circulation was rendered more active in the limbs, exhibiting large red patches, more intense in the vicinity of the punctured region. This condition would last three and even four days after the operation. The injections were attended with perspiration of the head and limbs, more profuse with the girl than with the boy. The pupils were always dilated, and gurgling of the bowels would persist some minutes after the puncture. Another very perceptible result was the fibrillar contractions, or twitching of the muscles in the limbs, lasting for a minute or two, and which I have found prolonged for more than an hour in other similar cases."

When we come to analyze the symptoms produced by the subcutaneous injection of strychnia, we perceive that the action is exerted chiefly on the nervous systems of animal and organic life.

Dr. Echeverria, from whose able paper I have just quoted, makes much of the effects on the organic nervous system to support his peculiar views of the nature and causes of certain forms of paralysis. These effects are the following:

The dilatation of the pupil.

The intestinal movements.

The sweating.

The rise in temperature of the paralyzed parts into which the injection has been inserted.

There are no differences of opinion as to the action of strychnia on the nervous system of animal life; but the special seat of the action is much disputed about. It would be of little service to occupy space with these different opinions; it will suffice to state that Schroeder Van Der Kolk has demonstrated in a conclusive way that it acts on the medulla oblongata, the alterations of this organ consisting in a dilatation of its minute vessels. The morbid state of the reflex faculty is a product, then, of the altered nutrition of this part of the cord.

In addition to these remote effects of the injection consecutive to absorption, it is important to note certain local effects of a special kind, of great importance from the point of view of the therapeutical action of strychnia in paralytic affections. Dr. Echeverria has called attention to the "fibrillar contractions, or twitchings of the muscles in the limbs" into which the strychnia injection has been thrown. I have witnessed this very satisfactorily in the course of some experiments with atropia and strychnia simultaneously injected. If a mixed atropia and strychnia injection be thrown under the skin of a cat, dilatation of the pupil will quickly occur, followed by violent twitching of the muscles in the neighborhood of the injection, and thence propagated to all the voluntary muscles.

THERAPY.—The hypodermic use of strychnia is based upon the physiological action of that agent, and I consider its therapeutical application from this point of view.

In Paralysis.—Dr. Béhier, of Paris, appears to have been the first to use the hypodermic injection of strych-

nia for the cure of paralysis. Prof. Courty afterward used it in three cases of facial palsy, the patients completely recovering. The most important contribution to our knowledge on this subject was made by Mr. Chas. Hunter, in a paper entitled "On Strychnia Hypodermically Administered in Paralytic Affections."* The paper of Dr. Echeverria, from which I have quoted, has also advanced our knowledge. The forms of paralysis which have been treated in this way, are the following:

Hemiplegia.	Infantile paralysis.
Paraplegia.	Local paralyses.

Progressive muscular atrophy.

Progressive locomotor ataxia.

Mr. Hunter reports three out of four cases of *hemiplegia* cured by the injections of strychnia. Two of the cases were respectively of six and two and a half years' duration. This statistical statement should not mislead the reader. Success like this cannot be expected in the treatment of paralysis of cerebral origin; the cases of Mr. Hunter were evidently very favorable cases for treatment by this method. Nevertheless, the hypodermic injection of strychnia, in many cases, is decidedly curative. As Dr. Echeverria has well remarked, "the effects of strychnia are widely different when administered hypodermically or by the mouth. By the latter method, the quantity may be repeated and increased, unsuccesfully, as manifested in the cases of Hunter, and in those here related, and yet a

* British and Foreign Medico-Chirurgical Review, April, 1868.

smaller dose of the substance, exhibited hypodermically, be capable of regenerating at once the lost muscular power."

We should possess clear notions, then, as to the circumstances in which it may be proper to use the hypodermic injection of strychnia in hemiplegia, for, manifestly, a remedy of such power may prove to be as harmful when indiscreetly used as it is unquestionably useful in suitable cases.

It is contraindicated in recent hemiplegia.

In my own experience it has not been useful in old cases characterized by contractions of the palsied limbs, for this condition signifies, according to Todd, who styles it "late rigidity," an irritative action about the site of the extravasation.

It has been exceedingly useful in old cases of hemiplegia in subjects not very advanced in life, the paralysis being partial as to motility, and the limbs not wasted.

The hypodermic injection of strychnia has been used in *spinal paraplegia* by Béhier, Courty, Ruppaner, Hunter, Echeverria, and others, with success. The rules for its administration are similar to those I have given for hemiplegia.

It is not proper in acute cases involving structural alterations of the spinal cord.

In cases of paraplegia due to softening or tumor in the spinal canal it will do harm.

It will be beneficial in cases of reflex paraplegia, in paraplegia due to anæmia of the cord, in hysterical paraplegia, and in those cases of paresis of the muscles of the inferior extremities due to concussion of the cord, but after the acute symptoms have subsided.

It is certainly true, however, that Mr. Hunter obtained advantage from it in a case the symptoms of which indicated myelitis. Dr. Echeverria's Case I. may be classed in the same category,—the patient complaining of formication and numbness, and being paralyzed both as to motion and sensation.

The hypodermic injection of strychnia has proved an exceedingly valuable adjunct to the treatment of *infantile paralysis.* If the electro-muscular contractility to the continuous or induced current be not lost, very beneficial results may be expected from this treatment. The injection promotes the capillary circulation, and increases the growth and power of the muscles.

In various *local paralyses* the hypodermic injection of strychnia is even more decidedly curative. Courty* cured *facial paralysis* by injecting strychnia over the course of the facial nerve. Pletzer, Lorent, Sacmann, and Eulenberg had good results from the same treatment.† In a case of paralysis of the vocal cords with aphonia, Neudörfer failed, but in a similar case Waldenburg succeeded with the strychnia injection.

In the "drop wrist" of lead poisoning—*paralysis of the extensors*—it is a very important addition to the other means of treatment of this very obstinate affection. It is more successful than any other agent in *writer's cramp.* Palsy of single muscles or groups of muscles, following cold or rheumatism, is generally curable by this means. The injection also increases much the contractile power in cases of palsy following injury of nerve trunks.

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* Eulenberg, p. 243. † Ibid.

Paralysis of the bladder, with dribbling of urine, and *paralysis of the sphincter ani* not due to myelitis, are much benefited and frequently cured by this means.

In *progressive muscular atrophy* it has been used with great advantage in cases in which the electro-muscular contractility was not lost.

In paralysis of cerebral or spinal origin, without wasting of the muscles, the injection may be made under the skin. The dose of strychnia will vary, with the age of the subject, from $\frac{1}{60}$ to $\frac{1}{10}$ of a grain. In local paralyses, in infantile paralysis, in progressive muscular atrophy, the injection must be made into the affected muscles. If the electro-contractility be not lost, the following effects may be expected:

Rise in temperature of the limb, and increase of capillary circulation.

Increase in muscular power with growth of muscles.

Cure of the paralysis.

If, however, the electro-muscular contractility is lost, fatty degeneration has so far proceeded that the injection of strychnia will be useless.

The method of practicing the injection into the muscles is as follows:

The affected muscle or group of muscles is grasped with the left hand and made prominent, and with the right the needle is plunged quickly and boldly into the muscular tissue. When inserted as far as necessary, withdraw the needle a short distance and inject slowly. It is important, of course, to avoid the blood-vessels, and to insert the needle into the paralyzed muscles. The pain of this operation is not greater than the subcutaneous injection, and little danger of

deep-seated abscess is to be feared. Muscular tissue, as is well known, does not readily take on the morbid action called inflammatory. The systemic effects do not follow so quickly nor are they as powerful after injection into the muscular tissue as after the subcutaneous injection. Both local and systemic effects are produced; but it is chiefly the local effects which are desired in cases of local paralysis. Some cases of local paralysis, as of the bladder, cannot be reached in this way. In paralysis of the sphincter ani the needle may readily be thrust into this muscle.

The subcutaneous injection of strychnia has been used in *progressive locomotor ataxia*, but with a negative result. In my own experience I have observed no decided influence for good or evil.

Neuralgia.—The hypodermic injection of strychnia has been used by Dr. Anstie in *gastralgia* and *cardiac neuralgia*, with advantage. "My decided opinion is, at present," says Dr. Anstie, "that there is no such remedy for gastralgia as strychnia, subcutaneously injected in doses of $\frac{1}{120}$ to $\frac{1}{60}$ of a grain." Although I cannot speak so positively as Dr. Anstie on this subject, I can say that I have observed good effects from the strychnia injection in the class of cases to which he refers.

As a Tonic.—I have used the subcutaneous injection of strychnia to overcome the depression caused by the withdrawal of morphia. It has also given much relief in cases of violent nausea and vomiting produced by the morphia injection.

Treatment of Strychnia Poisoning.—As accidents may happen in the use of strychnia by subcutaneous

injection, it is well to be prepared with the best measures for relief. For the toxic symptoms which occurred in his cases, Dr. Echeverria employed the inhalation of ether, and a turpentine clyster. The elaborate experiments of Dr. Fraser with Calabar bean have shown that we possess in this agent a complete physiological antagonist to strychnia. The physician who uses toxic doses of strychnia against paralysis, should be provided with a solution of the extract, or of eserine, the active principle. In the absence of this, the inhalation of ether, employed successfully by Echeverria, should be used. No reliance can be placed on the subcutaneous injection of atropia, for, as I have experimentally shown, this is not a physiological antagonist to strychnia. Atropia does not abolish the reflex faculty in animals poisoned by it,—a fact affirmed by Lemattre and verified by myself. It should not therefore, as done by Gubler,* be included among the physiological antagonists of strychnia.

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* Commentaires Thérapeutiques du Codex Medicamentarius, p. 599. Paris, Bailliere, 1868.

V.

CONIA.

The Solution and Dose.—The formula of Eulenberg is as follows:

℞.—Coniæ, gr. ss;
Spiriti, ʒss;
Aquæ dest. ʒiss. M.

Five minims of this represent one-forty-eighth of a grain. In preparing this solution, the conia should be first dissolved in the spirit, as it is insoluble in water. It is volatile, and exceedingly liable to decomposition, being converted into ammonia and a resin. For these reasons the solution should be prepared for use when required.

The dose will range from $\frac{1}{120}$ to $\frac{1}{60}$ of a grain: 2 to 4 minims of the solution above given.

Physiological Effects.—The local effects of the injection are the same as those of other alkaloids. In the largest dose which can be safely administered, it induces sleepiness, vertigo, coldness of the surface, diminished sensibility, and weakness of the inferior extremities. The respiration becomes slower, and less full. The pulse diminishes in number and force, falling so much as thirty to forty beats per minute.

In a case of poisoning carefully observed by Dr.

Bennett,* weakness of the legs, and staggering, were first noticed. Loss of all power of voluntary movement next followed. He became unable to swallow, and completely lost his power of vision. "His pulse and breathing were perfectly natural," but at the expiration of a half-hour after this, paralysis of the muscles of respiration had taken place, the action of the heart continuing but was "very feeble." Meantime his intelligence was preserved, but he was without power of articulation.

The mode in which conia produces these effects has been elaborately examined by Kölliker and Guttman. The last-named observer has shown that conia does not act on the spinal cord, nor does it destroy the irritability of muscle, but paralyzes the peripheral terminations of the motor nerves. Death is produced by asphyxia—paralysis of the muscles of respiration—and not by cessation of the heart's movements, for these continue after respiration has ceased.

THERAPY.—The therapeutical applications of conia by the hypodermic method are neither numerous nor important.

It has been used in the treatment of *asthma* by Pletzer. Although it appears to be a rational remedy, paralyzes the muscles of respiration, and in this way may be supposed to antagonize that condition of things which exists in asthma, experience is not in its favor; and a careful examination of its physiological effects discloses the fact that the influence which it exerts on respiration is a toxic action only. In the treatment

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* Clinical Medicine, p. 413, Am. ed.

of asthma it is not at all equal to morphia and atropia; nevertheless, in cases in which these agents disagree, or in which it is undesirable to use them, it may be tried.

Erlenmeyer procured relief by the hypodermic injection of conia to the difficult breathing of *emphysema.* The same authority reports having cured a case of *angina pectoris,* by two injections of conia. He therefore recommends it in these affections.

Lorent, influenced by theoretical considerations,—the action of conia on the pulse and respiration,—has employed this agent hypodermically in pneumonia and pleuritis, with the effect to reduce decidedly the pulse rate. It does not appear that this treatment is worthy of serious consideration. In the spasmodic affections of the thoracic viscera, Lorent has had experiences with conia similar to those of Erlenmeyer.

Conia is also one of the numerous remedies proposed for the cure of *tetanus.* Successful cases have been reported, cured by conium administered internally, but we may be permitted to distrust these, since Harley has shown that the extract is entirely devoid of conia, and therefore innocuous. For the treatment of tetanus, the hypodermic injection of conia may be used with a reasonable expectation of benefiting the patient.

As conia produces motor paralysis, it has been held to be an *antagonist to strychnia;* but since it has been shown by Guttman that conia paralyzes the peripheral terminations of the motor nerves, and does not act upon the cord, this view must be abandoned.

VI.

WOORARA.

The physiological effects of woorara are similar to those of conia. It paralyzes the motor nerves, commencing at the periphery, and produces death by asphyxia, without affecting the action of the heart.

These physiological effects, determined by Bernard, Kölliker, Kühne, and others, have led to its use in certain disorders of the nervous system in which the reflex faculty is abnormally excited. When the first publications were made, setting forth its peculiar action, very confident hopes were entertained that a specific for *tetanus* had been discovered. It failed in the hands of Follin, Gintrac, Cornoz, and Richard, and was successful in the hands of Gherini, Demme, Lochner, and Spencer Wells.* In most of the successful cases it was used endermically as well as hypodermically. Of twelve cases treated by the hypodermic injection, four terminated favorably. According to the statistics of Demme, of twenty-two cases treated by woorara, administered in either mode, eight recovered. Prof. Busch treated eleven cases of tetanus by woorara, and six recovered; but, as the professor thinks this agent is adapted only to the more chronic cases, our estimate

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* Eulenberg, op. cit.

of the value of this remedy must not be too high, for chronic cases often terminate in recovery under the most diverse methods of treatment.

In the successful cases, large doses of woorara were administered. Spencer Wells injected one-twelfth of a grain at a dose. The dose ranges from one-sixtieth to one-thirtieth of a grain. The frequency of administration will be governed by the effects upon the spasms.

Woorara has also been used in *epilepsy*, in *convulsive tic*, in *strychnia poisoning*, but without sufficient success to justify its employment in this class of cases. It does not bear the relation of a physiological antagonist to strychnia, and hence should not be used against the toxic symptoms caused by this agent.

VII.

NICOTIA.

The Solution and Dose.—Erlenmeyer recommends the following formula :*

℞.—Nicotiæ, gr. ss ;
Aquæ destil. ʒij. M.

Four drops (minims) of this contain one-sixtieth of a grain—a suitable dose.

Physiological Effects.—Nicotia is one of the most deadly poisons, ranking in this respect with prussic acid. In its local action it is somewhat irritant. In its remote or systemic action it strongly depresses the nervous and vascular systems. At first respiration is slightly accelerated, and is accompanied by a bruit, produced, according to Bernard, by a very abrupt contraction of the diaphragm. Slowness and feebleness of respiration soon succeed to this acceleration. The pupils dilate, and convulsive phenomena make their appearance in the eyes and extremities, partly of a clonic, and partly of a tonic or tetanic character. Complete adynamia supervenes, accompanied by muscular trembling ; the action of the heart becomes exceedingly

* Die Subcutanen Injectionen, op. cit. p. 85.

feeble, and death takes place by failure of the circulation (paralysis of the heart).*

THERAPY.—Nicotia has been employed with success in the treatment of *tetanus*. About one-half of the traumatic cases treated with it get well—a proportion of recoveries greater than with any other remedy except physostigma.

Prof. Houghton, of Dublin, who was probably the first to employ this agent in tetanus, ascertained experimentally that it is a physiological antagonist to strychnia.

Nicotia is indicated in *spasmodic asthma*, certain cases of *angina pectoris*, *colic*, *strangulated hernia*, etc., but I know of no instance in which it has been used for the relief of these conditions.

Cases of obstinate *convulsive tic*, "*histrionic spasm*," and local *muscular spasm* are of a nature, theoretically speaking, to be benefited by the subcutaneous injection of nicotia.

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* Gubler, Commentaires du Codex Méd., op. cit. p. 347.

VIII.

HYDROCYANIC ACID.

The Solution and Dose.—The *Acidum Hydrocyanicum Dilutum* of the U. S. Pharmacopœia is the preparation which I have employed for hypodermic use. The maximum quantity which I have used is four minims, but this amount is hardly safe in many cases. It should not be forgotten that the action of hydrocyanic acid is so rapid that a toxic dose introduced under the skin would infallibly destroy life before any measures could be employed for relief. For ordinary purposes, two minims of the officinal solution will be sufficient for hypodermic use. As its effects are quickly expended, it may be repeated frequently.

Physiological Effects.—Locally, the effects are somewhat irritant, but are not more so than a solution of morphia. A metallic taste, slight salivation, faint nausea, giddiness, and sighing respiration are the only systemic effects which I have observed from the doses I ventured to administer.

Therapy.—The good effects sometimes produced in *mental disorders* by prussic acid, when administered by the stomach, are more conspicuously exhibited when the remedy is injected under the skin.* It is

* McLeod, Medical Times and Gazette, March, 1863.

adapted to acute cases, in which power is in excess. Cases of mania or melancholia, in which the subcutaneous injection of morphia proves hurtful, are benefited by prussic acid, and *vice versa*.

I have used hydrocyanic acid hypodermically in spasmodic asthma, but without moderating the paroxysms. It is indicated in *angina pectoris*, and other cardiac neuroses, but I am not aware of any instances in which it has been tried.

As a remedy for *gastralgia* when a simple neurosis of the stomach, it is undoubtedly useful. In *nausea* and *vomiting* due to functional disturbance, and especially those cases in which morphia and atropia disagree, it may be used with a confident expectation of affording relief. But, as a general practice, the subcutaneous injection of prussic acid in those stomach disorders is, in respect to promptness and efficiency, greatly inferior to morphia and atropia.

The injection may be practiced over the epigastrium in cases of vomiting.

W. Preyer,* who has carefully investigated the physiological action of prussic acid, affirms that atropia is a physiological antidote. His researches have conducted him to the conclusions that prussic acid acts by depriving the blood of its oxygen, and that in very large doses it paralyzes the heart. He considers atropia the antagonist to this action by maintaining the action of the heart. I have carefully repeated the experiments of Preyer, and am unable to confirm

* The Practitioner, vol. i. p. 106.

them.* I find that animals (cats) fully under the influence of atropia are speedily destroyed by poisonous doses of prussic acid—just as speedily, indeed, as if atropia had not been administered. If administered simultaneously, or atropia soon after prussic acid, the result is the same.

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* Prize Essay of American Medical Association, for 1869, on Atropia.

IX.

PHYSOSTIGMA.

The Solution and Dose.—The following formula may be used:

℞.—Ext. physostigmæ, gr. ij;
Aquæ destil. ʒi.
M. Filter.

Ten minims of this solution contain $\frac{1}{3}$ of a grain, a sufficient quantity to commence with. As Dr. Fraser remarks,* arbitrary rules for the dosage cannot be laid down. As the solution of the extract has an acid reaction and produces irritation of the tissues, it should be neutralized by carbonate of soda.

The alkaloid *eserine* may also be used, but as it is an unstable preparation the extract should be preferred. I have used, in some investigations of my own, an alkaloid prepared by Merck of Darmstadt, to which he affixed the name "calabarin." Although this has the properties of physostigma, it cannot be considered a pure alkaloid.

The solution of the extract should be prepared when it is needed, since it decomposes after a time.

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* The Practitioner, vol i. p. 85.

PHYSIOLOGICAL EFFECTS.—In a short period the pupils begin to contract. This corresponds in point of time with contraction of the ciliary muscle and change in the curvature of the lens, whence the patient becomes myopic. This change in accommodation produces a distinct sensation—a feeling of tension in the eye. A feeling of weight and tension in the head, giddiness, nausea, muscular feebleness and trembling, pale and cold skin, sweating, feebleness of the pulse, vomiting and catharsis are observed generally in the order I have named them.

A toxic dose produces in animals complete muscular relaxation. According to Fraser, to whom we are chiefly indebted for the present knowledge on this subject, toxic doses in man cause sudden and intense thirst; deglutition becomes difficult and the saliva dribbles from the mouth; slight convulsive movements take place chiefly in the muscles of the back, and death occurs in about thirty minutes. Dr. Fraser ascertained the following facts with regard to the modus operandi of Calabar bean:

It destroys the sensibility of the motor nerves, but does not affect the irritability of muscle.

It heightens rather than diminishes the sensibility of the sensory nerves.

It acts on the spinal cord, destroying its reflex power.

It does not affect the brain—consciousness in animals and the intellect in man remaining unimpaired.

It enfeebles the action of the heart, diminishes the number of contractions, and lessens the duration of the

systole. This action is exerted through the influence of the poison on the cardiac ganglia.

By paralyzing the muscles of respiration, it frequently produces death by asphyxia.

THERAPY.—The therapeutical applications of physostigma have been deduced from its physiological effects. Dr. Fraser, who made the elaborate study of the mode and character of its actions, indicated from these the direction of its therapeutical utility.

Of all the remedies which have been proposed for *tetanus*, physostigma must be regarded as the most useful. Soon after it was suggested by Dr. Fraser for the treatment of this disease, it was tried by M. Lemaire, in whose hands it proved successful. Dr. Fraser publishes* a list of eleven cases in which physostigma was used: nine of these recovered and two died. Success so extraordinary as this has not continued. Thus Dr. T. H. Kearney† of Cincinnati, in an excellent statistical summary of the effects of remedies in tetanus, shows that of thirty cases of tetanus treated by Calabar bean, eighteen recovered and twelve died.

It is certainly true, however, that all cases treated by Calabar bean were not managed with equal judgment and skill. Dr. Fraser has indicated the mode in which physostigma should be used. In order to be successful, the precautions which he suggests should be heeded. I can therefore do no better than transcribe the observations he has made on this subject.

"I should myself feel inclined always to commence

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* The Practitioner, vol. i. p. 83.

† Cincinnati Lancet and Observer, September, 1869.

the treatment by subcutaneous injection, and to repeat such injection until the system is decidedly affected, and then to administer the remedy by the mouth, in a dose three times as large as is found necessary by subcutaneous injection. Such a plan might be quite safely followed in a child of even nine years. If the remedial effects continue to be produced by administration by the mouth, it should be persevered with, for such administration has obvious advantages as far as the convenience of the practitioner is concerned. In the more severe cases, however, I believe subcutaneous injection should be alone employed. The distress and increase of spasm caused by swallowing, or the impossibility of introducing substances by the mouth, will render this necessary. I cannot also too strongly urge that subcutaneous injection should always be used when severe and continued spasms occur, when a fatal result is imminent from the exhaustion caused by prolonged and frequent convulsions, and when apnœa threatens at once to close the tragic scene. By it we obtain the quickest and most powerful effect.

"From the preceding remarks, it cannot be expected that any arbitrary rules of dosage can be laid down. For an adult, one grain of the extract by stomach, or one-third of a grain by subcutaneous injection, will generally be sufficient to commence with. This should be repeated in two hours, when its effects will usually have passed off, and the succeeding doses may be modified according to the experience that will thus be gained. * * The great object is to produce as quickly as possible, and then to maintain, the physiological effect of physostigma in diminishing reflex excitability.

The doses must, therefore, be continued in increasing quantities until this physiological effect is produced, or until the sedative action of the drug on the circulation is carried to a dangerous extreme, or until constant nausea and vomiting compel us to desist."

Physostigma is the true physiological antagonist of *strychnia*. While strychnia exalts, physostigma destroys the reflex faculty of the cord. By experiments on animals, Dr. Fraser determined that the toxic symptoms produced by strychnia were relieved by physostigma.

In tetanus, as in strychnia poisoning, the signs of relief afforded by physostigma are the following:

The immobility and rigidity of the muscles of the extremities disappear and the muscles become flaccid and freely movable. The abdominal muscles also lose their rigidity and the opisthotonos disappears.

The pupils contract.

The pulse falls.

Physostigma has also been used for the cure of *chorea* by Dr. George Harley and Dr. John Ogle. In these cases it has been prescribed by the mouth, and no necessity appears to exist for its administration by the hypodermic method.

X.

CAFFEIN.

The Solution and Dose.—The solution recommended by Eulenberg is prepared according to the following formula:

℞.—Caffeini puri, gr. vj;
Spirit. vini,
Aquæ destil. āā ʒi. M.

Twenty minims of this solution contain one grain of caffein.

Lorent's formula is as follows:

℞.—Caffein. citrat. gr. i;
Glycerina pur. gtt. xxiv. M.

One grain of caffein is the usual dose for subcutaneous injection.

Physiological Effects.—The local effects are similar to those produced by the other alkaloids. Slight drowsiness is first produced, but this is soon followed by stimulation of the brain and other animal functions. In very large doses it produces decided excitement of the nervous and vascular systems, violent palpitation of the heart, with frequency, irregularity and sometimes intermittence of the pulse, oppression and pain in the head, disorders of the senses, ringing in the ears, flashes of light before the eyes, priapism, and delirium

THERAPY.—Caffein has been used hypodermically for the relief of *neuralgia.* Eulenberg found advantage in it, in a case of occipital neuralgia. Dr. Anstie says with regard to it: "In one instance of severe neuralgia of the superficial branches of the circumflex in the shoulder, two successive injections of caffein (over the biceps) appeared to cut short the malady altogether. In a case of dorso-costal neuralgia, attending shingles, the patient was injected daily for five or six days, with the effect of notably mitigating the pain on each occasion."

Lorent used the hypodermic injection of caffein in *hysterical headache* and *migraine.* Dr. Anstie relieved by it the insomnia attendant upon chronic alcoholism without delirium. In these affections, caffein, as Dr. Anstie suggests, will probably be found a valuable remedy.

This remedy is indicated in simple melancholy, in hysterical seizures, in certain cases of delirium tremens; but our knowledge of its applications is not yet in a sufficiently advanced state to pronounce positively upon these points. It has also been used with success against *opium narcosis;* in this it is certainly inferior to atropia, yet as there is no *therapeutical incompatibility,* these agents may be used at the same time.

XI.

ERGOTIN.

The Solution and Dose.—Eulenberg gives the following formula:

℞.—Ergotini, gr. ij;
Spir. vini rect.
Glycerini puri, āā ʒss. M.

Five minims of this contain $\frac{1}{6}$ of a grain. The aqueous extract of ergot, or *Bonjean's ergotin*, is more usually employed in the dose of $\frac{1}{4}$ of a grain dissolved in distilled water. The fluid extract (U. S. P.), carefully filtered, may be injected in the dose of 10 minims.

Physiological Effects.—The symptoms of acute ergotism are the following: nausea and vomiting, abdominal pain, diarrhœa, dryness of the throat, thirst, anorexia; itching of the extremities, numbness, lassitude, vertigo, dilatation of the pupils, drowsiness, delirium and stupor; diminution of the force and frequency of the pulse (rarely the reverse), with tendency to syncope, pallor and lividity of the face. (*Gubler.*)

The action of ergot is chiefly expended on the organic nervous system. According to Brown-Séquard, by causing contraction of the muscular fiber of the arterioles, it produces anæmia of the nervous centers. If this be the correct view, the toxic phenomena referrible to the nervous system of animal life are consecutive, and not due to the direct action of the agent on

the brain and cord. This view is probably too exclusive.

The hypodermic injection of ergotin, in suitable doses, will not cause the symptoms of acute ergotism above described, but a knowledge of the symptoms which may be looked for when it is desired to push the remedy, is necessary in order to avoid ill results.

THERAPY.—The hypodermic injection of ergotin is indicated when prompt contractions of the uterus are required, as in *post partum* hemorrhage.

Some very important results have lately been obtained by Langenbeck* in the treatment of *aneurism.* Recognizing the action of ergot in promoting the contractions of organic muscular fiber, Prof Langenbeck bethought himself that this same action might be usefully applied in the treatment of aneurism. His first experience was in a case of subclavian aneurism. He injected thirty grains of ergotin (aqueous extract) in the space of forty days, which procured great relief, diminishing the size of the tumor, and the pain and paralysis of the arm and hand. A radial aneurism was quickly cured by the same means, viz., the injection under the skin, over the tumor, of a solution of aqueous extract of ergot.

Profuse and alarming *epistaxis*, *hemorrhage* in cases of the hemorrhagic diathesis, and *metrorrhagia* are conditions of disease in which the subcutaneous injection of ergot may prove of great utility. I have, however, no experiences to offer as respects the use of the agent hypodermically in these cases.

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* Berlin. Klin. Wochensch., 2, 1869. Quoted in the Practitioner, vol. ii. p. 311.

XII.

QUINIA.

The Solution and Dose.—The solution for subcutaneous use which I have recommended* is the following:

℞.—Quiniæ sulphat. ʒi;
Acid. sulph. dil. ♏xl;
Aquæ destil. ʒi. M.

This should be carefully filtered, to separate any particles of undissolved quinia or foreign matter. From 15 to 30 minims of this is a sufficient dose. It should be injected into a place where the areolar tissue is abundant. If a larger quantity than 30 minims be necessary, it were better to insert in two places. As ether is a good solvent of the alkaloid *quinia*, the following may be used:

℞.—Quiniæ, gr. viij;
Ether, ʒi. M.

Or, shake together any convenient quantity of quinia (the alkaloid) and ether; one part of the former will be taken up by sixty parts of the latter. The ether being allowed to evaporate spontaneously, a solution may be obtained, finally, of one part of quinia to six parts of ether. This solution is in some respects objectionable: the rapid evaporation of the ether leaves

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* Russell Prize Essay on Quinine.

the quinia an adhesive mass, which occludes the syringe and makes the injection difficult and uncertain.

Physiological Effects.—The solutions of quinine, when injected beneath the skin, excite considerable burning and a zone of more or less intense redness for some distance around the puncture. If care be not used in the preparation of the solution, inflammation will follow at the site of the puncture, matter will form, and possibly a diffuse inflammation of the areolar tissue will ensue. Before I had learned the necessity for caution, accidents of this kind occurred in my own hands, and lately some very bad cases have been reported as occurring at New Orleans, where, it is said, a *mixture* of quinia sulphate and water was injected under the skin.

Very slight systemic effects follow the subcutaneous injection of quinia. They are similar in character to those produced by the stomach administration, and, as they are so well known, require no description here.

Therapy.—"Dr. Chasseaud published, in 1862, an account of the great success which he had obtained in the treatment of *malarial fevers*, in the hospital at Smyrna, by the subcutaneous injection of quinine. He ascertained that this agent, administered in this way, had a more decidedly curative power, without occasioning its usual physiological effects, than when given by the stomach. This practice has since been continued with undiminished success at the same hospital by Dr. J. McCraith."* Dr. Moore, of the Bom-

* Extracted from my Prize Essay on Quinine.

bay Medical Service, repeating these experiences, concludes "that four or five grains of quinine injected beneath the integument are equal to five or six times that amount taken into the stomach."

Not only is the immediate therapeutic effect of the quinine given in this way greater, but more permanent cures thereby result. In one hundred and fifty cases treated in this way, Dr. Chasseaud had but a single relapse. Such has been my own observation.

From three to five grains, injected under the skin, will suffice to cure an ordinary intermittent. Fevers of the remittent type, and pernicious fevers, will require a larger amount. In those deadly malarial attacks, known as *pernicious*, is the efficacy of this treatment most conspicuous. Much depends, as everybody knows, upon bringing the patient promptly under the quinine influence; the subcutaneous injection is the quickest and most powerful means of accomplishing this object.

Recent malarial fevers may be aborted at the beginning of the cold stage by a full injection, but it is better to anticipate the attack by an hour or two, in order to procure the physiological effects, before the onset of the expected paroxysm. It is true that the injection may be administered at any time during the febrile movement, but it is better to anticipate and prevent it. The ultimate cure will depend upon the amount of quinia received by the patient, and not upon the period at which it was administered.

The subcutaneous injection is much more effective also against *chronic malarial poisoning* than the stomach administration, but here we meet with new

conditions, requiring other management than the use of quinine. We may confidently expect to prevent the febrile movements by frequent repetition of the injection; but we do not thereby cure the disease, for the changes induced by the long-continued action of malaria, in the liver, spleen, gastro-intestinal mucous membrane, cerebro-spinal axis, must be corrected if we would arrest the objective phenomena of fever and cure the patient.

Dr. Eulenberg sums up his conclusions in regard to the cases in which the subcutaneous injection of quinia in malarial fevers may be desirable, as follows:

In intermittents complicated with gastric disorder.

In children in whom the disagreeable taste and the large doses necessary produce strong aversion and stomach derangement.

In poor and hospital practice, where economy in the use of the drug is desirable.

These conclusions seem to the writer well founded. But he has omitted chronic malarial poisoning, in which the subcutaneous injection of quinia has undoubted utility.

The hypodermic use of quinia has been extended to various diseases,—fevers, neuralgia, angina pectoris, strychnia poisoning, etc.,—but without advantage over existing methods of treatment.

Note.—Dr. Tessier, in the Mauritius, for the cure of intermittents injects under the skin a solution of *carbolic acid*, ¾ of a grain to 20 minims of water. He reports that the patients were rapidly cured!—*Lond. Chem. News*, July, 1869.

XIII.

MERCURY.

The Solution and Dose.—Applying the rules given in Part I., I reject all insoluble preparations of mercury. Scarenzio* used in 1864 a mixture of calomel, glycerin, and water. Hebra† injected a solution of sublimate—gr. i to ℥ss Aq. Hill of England made use of a solution of sublimate containing $\frac{1}{6}$ of a grain to the dose. Lewin,‡ who first submitted this practice to systematic examination, employed a weak solution of corrosive sublimate. The following is a suitable formula for hypodermic injection of mercury :

℞.—Hydrarg. chlor. corrosiv. gr. i;
Aquæ destil. ℥i. M.

Ten minims of this contain $\frac{1}{48}$ of a grain. As Lewin, and especially Liégeois, have shown that concentrated solutions are not desirable and that large doses are not necessary, this formula will be strong enough for ordinary purposes. Recognizing the fact that indura-

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* Eulenberg, op. cit. p. 307.

† Ibid. Also, Bulletin de Thérapeutique, vol. i., 1869, p. 297. De l'Application de la Méthode hypodermique au Traitement de la Syphilis par les Preparations mercurielles. Par le Dr. F. Bricheteau. Ibid., vol. ii. 1869, p. 158, by M. Liégeois.

‡ Ibid.

tion of the tissue, and frequently unhealthy and sloughing ulcers were produced by these injections of sublimate, Bricheteau requested M. Bouilhon, a Paris pharmaceutist, to prepare a salt of mercury soluble and free from irritant properties. M. Bouilhon suggested the double iodide of mercury and sodium as supplying the conditions required.

℞.—Hydrarg. et sodii iodid. gr. xxiv;
Aquæ destil. ℥iij. M.

Fifteen minims of this contain $\frac{1}{4}$ of a grain. Ten minims or $\frac{1}{6}$ of a grain will generally be sufficient for an injection. "This salt," says M. Bouilhon "fulfills perfectly the object; it introduces into the economy only the active substance combined with a small quantity of a salt of soda." But as this salt is difficult to prepare and as the corrosive chloride is more readily procured, the latter will generally be employed. With suitable precautions, abscess will not frequently result from its use. Thus, Lewin—who used his solution, which is stronger than that I have recommended—many hundred times, found small abscesses to occur in the proportion only of two to three for one hundred injections.

The formula of M. Liégeois,* whose very important memoir has just appeared, is as follows:

℞.—Hydrarg. chlor. corrosiv. gr. iij;
Morphiæ sulph. gr. iss;
Aquæ destil. ℥iij. M.

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* Bulletin Général de Thérapeutique, 30 Août, 1869, p. 158.

Fifteen minims of this solution contain $\frac{1}{32}$ of a grain, the quantity recommended by Liégeois for a single injection. It will be perceived that this solution contains the same quantity of sublimate as the formula I have proposed, but only about one-third of that used by Lewin. In two cases only has Liégeois observed abscess and eschar follow his injection. This comparative immunity from ill effects is to be attributed, unquestionably, to the small proportion of sublimate. The injection is preferably inserted under the skin of the back.

PHYSIOLOGICAL EFFECTS.—The injection of the corrosive chloride is accompanied by severe burning pain and considerable local heat and redness. If the solution be concentrated it will produce induration of the areolar tissue, inflammation and abscess, and sometimes a dry eschar, leaving an ulcer slow to heal. The intensity and persistence of the pain will depend upon the quantity of sublimate injected; weak solutions do not occasion much distress; the pain of any solution may be much mitigated by the conjoined use of morphia, as in the solution of Liégeois.

Salivation is frequently produced, according to Lewin, who had fifty-one cases of mercurial stomatitis in one hundred and forty-four men treated in this way. On the other hand, Liégeois found salivation an "exceptional" occurrence, there being only four in one hundred and ninety-six subjects, and these were mild cases. The difference in result here is plainly due to the difference in the strength of the respective solutions. It is a curious and important circumstance, that this physiological effect has no relation to the therapeutical

results in syphilis, for Liégeois' cures are even more numerous proportionally than Lewin's.

The subcutaneous injection of sublimate does not impair any of the functions, but increases the activity of the digestion and assimilation, so that decided increase in weight takes place in most of the cases in which it is employed.

THERAPY.—The therapeutical applications of mercury by the hypodermic method are confined to the treatment of syphilis, in which results of the greatest value have been obtained.

It is applied to the treatment of primary (infecting chancre), secondary (constitutional), and tertiary forms of this disease. I have used it with great advantage in the tertiary, but have not had the opportunity to give it sufficiently numerous and prolonged trials to enable me to pronounce as to its utility in primary and secondary syphilis. I therefore avail myself of the very full reports and statistical evidence published by George Lewin of Berlin, and M. Liégeois of Paris. The following are the statistics of Lewin:

"Cases* treated exclusively by injections of sublimate, 107; relapses 24, or 22 in 100.

"Cases treated by injections of sublimate, after sarsaparilla decoction and sweating, 58; relapses 19, or 30 in 100.

"Cases treated simultaneously by injections of sublimate, sarsaparilla decoction, and sweating, 24; relapses 7, or 33 in 100.

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* These statistics are based upon cases of constitutional syphilis.

"Cases treated by injections of sublimate and iodide of potassium, 60; relapses 14, or 23 in 100.

"Cases treated by injections of sublimate and chloride of potassium, 60; relapses 14, or 23 in 100."

To sum up—356 patients have been treated by injections of sublimate, either singly or joined to other means; the relapses have been 89, or 25 in 100.

With the ordinary means of treatment, the relapses are 81 in 100 cases.*

The conclusions arrived at by Lewin† as a result of his large observations, are the following:

1. The syphilitic phenomena disappear quickly, and with a rapidity proportional to the quantity of sublimate daily injected.

2. Certainty and precision of the method, as ascertained by nine hundred observations made during two years and a half.

3. Lessened number of relapses, and those that occur are light.

4. Facility of execution.

The statistics of Liégeois are even more favorable. Thus, of 196 cases of constitutional syphilis, treated by injections of sublimate, 127 were cured, and 69 were ameliorated. For the cured, the number of injections were 68; for those ameliorated, 50. The number of relapses in those noted as cured were 12 (9·45 in 100); for those noted as ameliorated, 14 (20·30 in 100). The greater number of injections, and the in-

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* Bulletin de Thérapeutique, vol. i., 1869, p. 300. Abstract of Lewin's researches by Bricheteau.

† Ibid.

creased length of time required by Liégeois' method, as compared with Lewin's, are due to the small quantity injected, but these disadvantages are more than counterbalanced by the greater proportional number of cures. The production of salivation, then, is unnecessary in order to secure the best results from the hypodermic injection of mercury. The longer the constitutional symptoms have existed, the greater the number of injections required to effect a cure.

In practicing the injection, the back should be selected for the site of the puncture. Two injections, of 8 minims each, may be practiced at one sitting, one on each side. This quantity should be inserted daily. If the symptoms be not urgent, if time is of little consequence, and if it be desirable to avoid salivation, the daily quantity may be much less.

I have purposely avoided all controverted questions in regard to the use of mercury in syphilis, simply stating the results which have been achieved by the hypodermic method. It is obvious that in all cases in which it is desirable to use mercury, the subcutaneous is the proper method for administering it. This is equally true of its use for the cure of infecting chancre as for constitutional syphilis.

Note.—In *Schmidt's Jahrbücher*, Band 142, Nr. 4, 1869, p. 39, Güntz has summed up the conclusions reached by Cl. Boese, R. Klemm, A. Merscheim, Dr. Grünfeld, and Dr. Stöhr. The experiences of the two last named are hardly so favorable as those of Lewin and Liégeois, but on the whole are satisfactory as regards the curative power of this method of treating syphilis. These observers appear to have used too large doses of sublimate, producing unnecessary accidents.

XIV.

ARSENIC.

The only observations on the subcutaneous injection of arsenic which I have been able to find, are a brief note by Eulenberg of the use of Fowler's solution by Prof. Lehman in a case of "pernicious puerperal fever," and in Reynolds's System of Medicine. In an article on chorea* in the latter work, Dr. C. B. Radcliffe has presented some interesting facts on this subject, which I subjoin.

"This patient had suffered for nine years with a distressing choreal affection of certain muscles of the neck, by which the head was kept continually turning and bobbing. At different times various modes of treatment had been tried, including the hypodermic injection of morphia and atropia, without the least benefit. * * The idea of injecting arsenic hypodermically occurred to me on the 12th of January, 1866, and was carried out the same day. Fowler's solution was chosen, and the part selected was the most tender point over the contracting muscle." Commencing with three minims, the quantity injected was finally raised to fourteen minims. "Before the fourth injection was practiced, a marked change for the better had taken

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* Vol. ii. p. 133, et seq.

place ; before the eighth, the choreal movements were almost at an end, and the change for the better had gone on steadily from the beginning." Dr. Radcliffe reports another case in which amelioration, equally as great, was produced by the hypodermic injection of arsenic, the patient being a lady sixty years of age. He has also employed "with results more or less satisfactory the hypodermic injection of arsenic in certain cases of neuralgia, epilepsy, and other affections of the nervous system."

In the choreal cases above referred to, Dr. Radcliffe's "object in introducing the arsenic hypodermically was not to escape gastric irritation, but to produce some local change in the nerves of the parts which were the seat of the disorder, as well as to bring about some more general change in the system."

Dr. Radcliffe employed for these injections at first the undiluted Fowler's solution, but as considerable local irritation followed he afterward diluted it by one-half water. This proved much less irritant. It is probable, I think, that the *Liquor Sodæ Arseniatis* will be found much better for hypodermic use than Fowler's solution. This being a higher oxide than the arsenite of potassa, is less irritant in its local action and less apt to produce arsenical poisoning. Moreover, it is a clear solution, possessed of a considerable degree of osmotic power. The solution of the arseniate of soda may be injected in quantities of five to ten, or even fifteen minims. Every alternate day is sufficiently often in ordinary cases to make the injection. It will be found advisable not to insert the solution frequently in the same neighborhood.

XV.

IRRITANT INJECTIONS.

Dr. Luton* of Rheims, under the singular designation "parenchymatous substitution," described a method of treating neuralgias, new formations, hypertrophies, etc. This method consists in the injection into the substance of the affected part of such irritants as tincture of iodine, nitrate of silver, chloride of sodium, etc. The term applied to this process was intended to express the theoretical views of its author in regard to the nature of the therapeutical action which takes place. The pain and irritation set up in the part were assumed to be *substituted* for the morbid process.

Dr. Ruppaner imitated this method of Luton in the treatment of sciatica and other neuralgias. Dr. Bertin (de Gray) also, attracted by the results obtained by Luton, practiced the method for several years and then published the results.† I have had myself a limited experience with this method.

The substances employed in this way are chiefly the following:

A solution of iodine.

A saturated solution of common salt.

A solution of the nitrate of silver.

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* Archives Général de Médecine, Oct. et Nov. 1863.

† Ibid., Avril, 1868, p. 444.

The tincture of cantharides.

The following is the solution of iodine employed by Bertin:

℞.—Potassii iodidi, gr. xv;
Tinct. iodinii, ʒijss;
Aquæ destil. ʒx. M.

The quantity of tincture of iodine he subsequently increased to ʒv.

The tincture of iodine is sometimes employed alone and undiluted.

The following is a suitable formula for the nitrate of silver solution:

℞.—Argenti nitrat. ʒij;
Aquæ destil. ℥i. M.

To illustrate at the same time the class of cases to which this method is applicable, and its therapeutical power, I subjoin the statistics of Bertin:

1. Tumors formed by development of the thyroid gland	8
Cured	5
Ameliorated	1
Failed	2
2. Lymphatic ganglions	3
Cured	3
3. Bursæ	1
Cured	1
4. Neuralgias	7
Old sciaticas treated by injection of nitrate of silver	2
Cured	2
Old sciaticas treated by solution of common salt	2
Cured	0
Recent sciaticas treated by solution of common salt	2

Ameliorated	2
Recent sciaticas treated by injection of nitrate of silver	1
Cured	1

Ruppaner employed the nitrate of silver injection in one case of cervico-brachial neuralgia, and in four cases of sciatica; two cases were ameliorated, and three cases of sciatica were cured.

As respects *neuralgia*, this method of treatment seems specially adapted to cases of sciatica,—obstinate cases in which structural alterations have probably taken place in the neurilemma. In order to be effectual, the injection—five drops of the nitrate of silver solution—should be thrown into the vicinity of the nerve. It produces great pain and burning, and is followed by considerable inflammation, not diffused, but localized to the site of the injection. Abscesses, of course, frequently happen from this practice, and, indeed, sufficient irritation to result in this way seems necessary to produce the best effects. It is probably true that the irritation, and not the agent, is the principal factor in the curative process.

Injections of the iodine solution have been practiced with success in *goitre*. The tincture of iodine may be thrown into the substance of an enlarged thyroid without producing violent irritation. Five minims of the tincture will be sufficient for this purpose, and it may be repeated every other day. Recent cases are quickly cured by this treatment. I have seen excellent results from the same application in those *cystic and glandular tumors* so frequently found in the cervical region. After evacuating the cyst with a trocar, the tincture of iodine may be freely thrown into the

sac, and the solid parts of the tumor injected by the hypodermic syringe, the needle point being well introduced into the substance of the growth.

Enlarged bursæ are best treated by the same means; evacuate the contents and inject the solution of iodine. Slight inflammatory action follows, the tumor becomes indurated, and finally disappears.

Solid tumors may be destroyed by injecting such irritants into them as will give rise to violent inflammatory action and sloughing. Into the substance of cancerous new formations, various corrosives may be injected, but this practice, although rational, has not hitherto proved satisfactory,—a remark equally true of Dr. Broadbent's method of injecting dilute acetic acid,—of the success of which such confident expectations were at first entertained.

Recently* considerable success has been claimed for the treatment of tumors by the injection into their intimate structure of *gastric juice.* As this practice is devoid of danger in suitable cases, and as the gastric juice is not difficult to obtain from the stomach of the pig, it is desirable to have further experience in order to form decided opinions as to its utility.

It would be foreign to my purpose to speak of such uses of the iodine solution as the injection in hydrocele, in hydrothorax and empyema, in cystic disease of the ovary, etc., and of the use of perchloride and persulphate of iron in nævus. These are subjects pertaining more especially to the domain of surgery, and have but slender connection with the subject of my work—Hypodermic Medication.

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* Bulletin Général de Thérapeutique, Août 15, 1869.

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